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BRONCHI AND BRONCHIOLI

By S. Engel
From the Department of Anatomy, The Royal College of Surgeons of England

Introduction

In order to arrive at a clear conception of the pulmonary structure it is necessary to consider the various constituents of the lung, viz.:

1. The respiratory tissue.
2. The air-conducting system (bronchial tree).
3. The glands attached to the bronchial mucous membrane.
4. Vessels, lymphatics and lymph tissue.
5. Interstitial and stabilising tissue.

The present paper is devoted to certain aspects of the bronchial tree, to particulars of its structure which may bear on normal respiration or be implicated in pathological processes. Bronchi and/or bronchioli may be the seat of acute or chronic processes so that knowledge of their structure is indispensable.

The lung is composed of a large number, between 30,000 and 50,000, of self-supporting units (acini). Each of the acini which, incidentally, are approximately the size of a medium bean, is supplied by a special " terminal bronchiolus," the last fully epitheliated one. The main bronchi split into large, medium and small bronchi and finally into several generations of bronchioli, the last of which is the terminal, " acinar " bronchiolus. The number of terminal bronchioli is the same as the number of acini. This fact alone points to the complexity of the bronchial tree as is demonstrated in Fig. 1 better than by any description.

The picture is taken from the side, from a cast (by courtesy of Dr. Tompset). The cast as reproduced is incomplete because the most peripheral elements have been pruned off to show the distribution of the large, medium and small bronchi. The enormous number of branches bears on the physical symptoms in disease and, in view of the many overcrossings, especially on the X-ray picture in pathological cases. Analysis of the mode of branching is not covered in this paper although it may be of some interest in the segmental nomenclature.

Bronchi and Bronchioli

Before turning to the histology of the bronchial and bronchiolar wall it is necessary to discuss first the intrinsic difference between bronchi and bronchioli. The customary classification refers to the calibre and to the presence or absence

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of cartilage; tubules less than 1 mm. in diameter, without cartilage in the wall, used to be called " bronchioli," but this classification does not consider the interrelationship between the pulmonary parenchyma and the air-passages.

The respiratory tissue is supplied by the bronchial tree so that every acinus receives air by a terminal bronchiolus. Several acini are united to form secondary lobules and these are limited by a connective tissue capsule. The secondary lobules are supplied by a bronchiolus of higher order and the lobular bronchiolus re-divides several times until the terminal, acinar bronchiolus is split off. The arrangement of lobular and terminal bronchioli gives the clue to the difference between bronchi and bronchioli (Figs. 2, 3, 4). Bronchi run within the septa radiating from the hilum and remain so to speak, extrapulmonary, using the septa as a kind of highway. The bronchioli, on the other hand, run within the parenchyma (Figs. 5, 6, 7, 8) in immediate contact with the respiratory tissue. Neither calibre nor cartilage but the situation, whether intra- or extrapulmonary, decides whether a tubule is bronchus or bronchiolus. That it is so can easily be seen in the lungs of young children or small animals, where cartilaginous bronchi with a diameter far below 1 mm., separated from the parenchyma, are quite common. The present differentiation between bronchi and bronchioli is coming to be accepted (Ham, 1957).

Histology of the Bronchial and Bronchiolar Wall

Before going into details I would like to stress that the air passages, bronchi and bronchioli, cannot and should not be considered as rigid tubes and tubules. They are to some extent rigid but are, at the same time, elastic. The smaller the passages are and the weaker, therefore, the stabilising fibrous tissue and cartilage, the more important this becomes. It is obvious that the bronchi must be kept patent in order to maintain the flow of air to the respiratory tissue. Patency is secured by the strong fibro-cartilaginous part of the wall. The larger the bronchi the stronger the cartilages. Near the hilum there are large plates (Fig. 4); they grow smaller and less numerous in the medium and small bronchi and vanish in the bronchioli. Incidentally, it may be mentioned that glands only occur in the bronchial wall as long as cartilage is present. Glands, therefore, are not part of the bronchiolar wall which is bare of cartilage.

Since the patency of the bronchi is mainly due to the strong fibro-cartilaginous portion of their wall, the question arises as to how the bronchioli are kept patent, considering their thin wall, lack of strong fibrous tissue and of cartilage. It is obvious that another mechanism must be at work. As a matter of fact the bronchiolar wall is to some extent stabilised by muscle and elastic tissue.

Elastica and Musculature

The fibro-cartilaginous layer of the *bronchi* contains many *elastic* fibres which are sometimes arranged into an inner and outer ring with many anastomoses between them. A much thinner layer is present in the tunica propria, that is to say in the smooth layer at the base of the epithelium. The bronchioli, on the other hand, only contain some weak elastic fibres throughout the wall, but

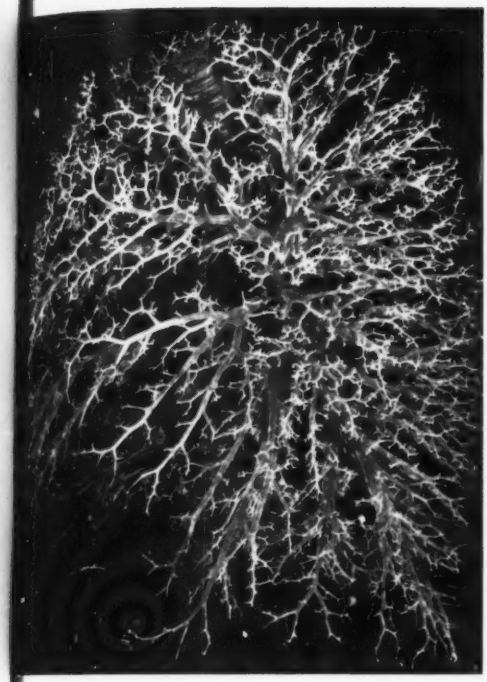

Fig. 1.—Cast of bronchial tree) ca. ½ life size. Photograph taken from the right.
(by courtesy of Dr. Tompset).

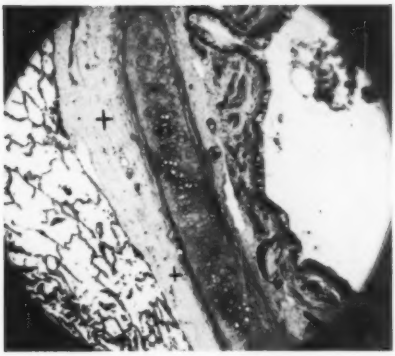

Fig. 2.—Part of a 3 mm. bronchus (adult). The septal tissue separating the bronchial wall from the respiratory tissue is marked by two crosses (×26).

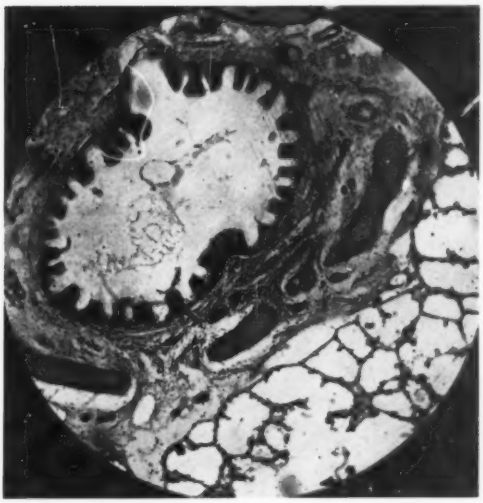

Fig. 3.—0·1 mm. bronchus of an infant showing all round the separation of the wall from the respiratory tissue (×45).

Fig. 4.—Part of a medium bronchus containing cartilage and glands (×45).

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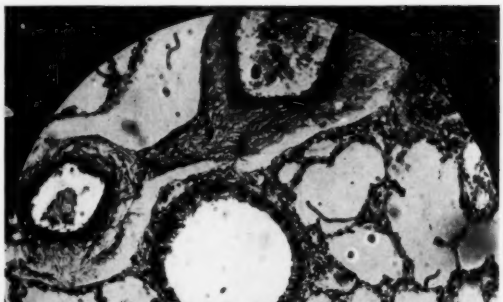

FIG. 5.—0·2 mm. bronchiolus within the respiratory tissue (×75).

FIG. 6.—0·4 mm. bronchiolus bearing ciliated epithelium, wall slightly infiltrated (×75).

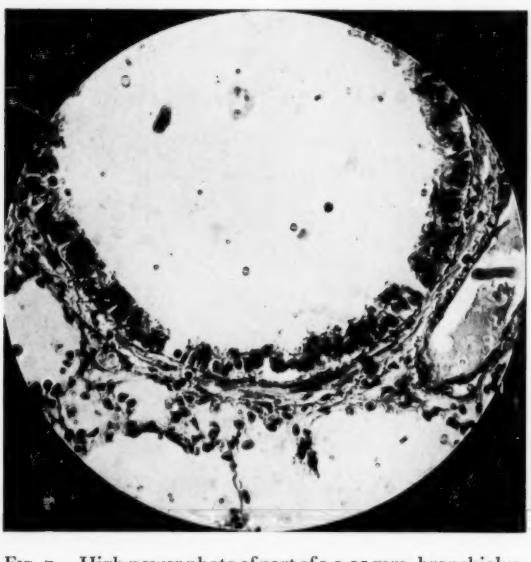

FIG. 7.—High power photo of part of a 0·25 mm. bronchiolus, marked contact with the respiratory tissue (×225).

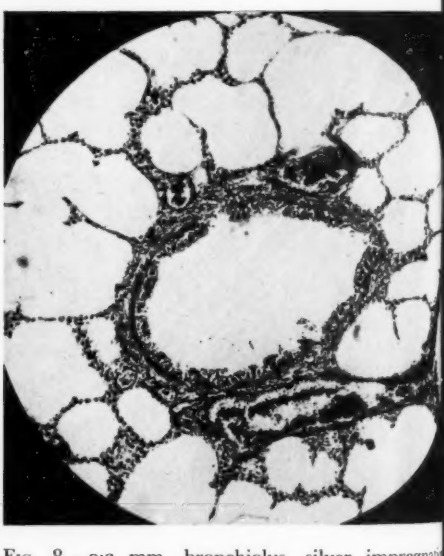

FIG. 8.—0·3 mm. bronchiolus, silver impregnation (×75).

below the epithelium, a well-defined elastic sheath is situated. Fibres of the sheath run mainly longitudinally but are connected by many anastomoses. The *muscle* also is different in bronchi and bronchioli. In the bronchi it is comparatively weak, mainly circular, and it functions as the motor of the mucous membrane. It does not affect the movements of the bronchi as a whole. Although very thin (approximately 0·05 to 0·02 mm.), muscle occupies a considerable proportion of the bronchiolar wall. The opinion has been put forward that the bronchiolar muscle serves to elongate and contract the tubule in inspiration and expiration. There is reasonable doubt that it is so. In my opinion, the muscle serves chiefly to stabilise the wall. Certain facts favour this conception, especially the strength of the muscle in various generations of bronchioli. It is commonly held that the muscle grows stronger the smaller the bronchiolus, but comparative measurements in children beyond the fifth year and in adults contradict this view, which is apparently due to an optical illusion. In truth, the ratio " diameter : muscle " is fairly constant, that is to say, the strength of the muscle grows with the bronchiolar diameter. The muscle in small bronchioli is more conspicuous than in large bronchioli, but the muscle in large is thicker than in small bronchioli. This fact alone suggests that the bronchiolar muscle serves less for movements of the tubule than for the prevention of collapse. Were the muscle to be arranged according to the former conception the large bronchioli might be liable to collapse. According to the present measurements the bronchioli of whatever calibre are likewise protected.

Movements of the bronchioli are likely to be passive, following the movements of the respiratory tissue with which they are intimately connected. This is especially true in inspiration, whereas in expiration the elastic sheath will help to restore the neutral situation between inspiration and expiration.

The Mucous Membrane (Bronchi)

The inner surface of the bronchi is lined by a comparatively thick mucous membrane; its various constituents are as follows:

1. Ciliated columnar epithelium, containing goblet cells.
2. Glands attached to the mucous membrane.
3. Basal layer of roundish cells.
4. Basement membrane.
5. Tunica propria plus elastica.

The mucous membrane of the bronchi serves various purposes. First, it keeps the bronchial surface moist and viscous. Dust and bacteria are trapped, removed towards the pharynx with the help of the cilia and finally expectorated. This function is greatly supported by the *folds* of the membrane, which obviously constitute a normal feature under physiological conditions. The folds increase the surface and the air is forced to pass through narrow channels between the folds (Figs. 9, 10, 11). It is obvious that the folded membrane works better than a membrane tightly adherent to the wall. The loss of folds occurs under pathological conditions, *e.g.* " chronic bronchitis " (Engel, 1958).

The bronchial mucous membrane rests on the tunica propria, a thin and loose layer of connective tissue (including elastic fibres) on which the membrane glides, the muscle being the motor of the movements. In the act of forming folds the tunica propria with its elastic fibres is drawn into the folds forming its core (Figs. 9, 10). The elastic tissue is therefore situated within the folds, wrongly giving the impression that the elastic tissue of the mucous membrane runs in longitudinal strands.

Apart from the cleansing function of the mucous membrane, its moistness provides all or a considerable part of the water which is necessary to keep the respiratory tissue moist.

The Mucous Membrane (Bronchioli)

Unlike the mucous membrane of the bronchi, that of the bronchioli is thin and not nearly so complex. Tunica propria and basement membrane vanish almost entirely, but the elastic fibres remain and constitute the above-mentioned elastic sheath. The epithelium consists of one low layer and gradually loses the cilia. There is no active function comparable with that of the bronchial mucous membrane.

Discussion

This paper desires to emphasise that neither bronchi nor bronchioli should be considered mere rigid tubes for the conduction of air to the respiratory units. On the contrary, the bronchial tree is an organ by itself, with active functions in physiological conditions and which may undergo pathological changes without implicating the lung. The peculiar properties of the bronchial tree are not yet fully known and this paper draws attention to the air passages, their function in physiological conditions and their potential pathological changes.

Summary

The bronchial tree is, within the lung, an independent organ. It serves primarily to conduct and moisten air passing to the respiratory tissue. The folds of the bronchial mucous membrane are a normal feature; they improve the function of the mucous membrane.

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FIG. 9.—Part of a bronchus with the mucosa in folds, the dark core is elastic tissue, stained red with Weigert: Saffranin-Resorcin (×26).

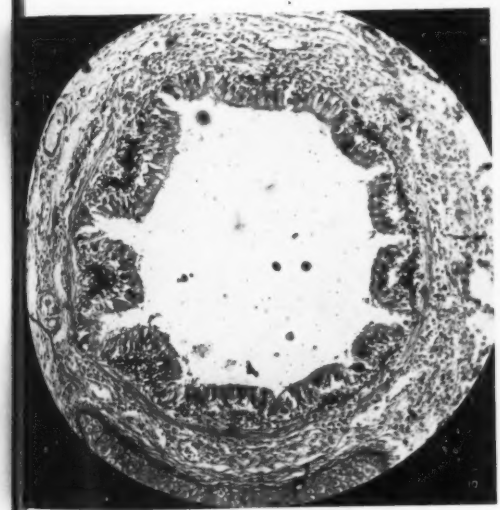

FIG. 10.—Small bronchus, stained like No. 9, showing folds with elastica almost all round (×75).

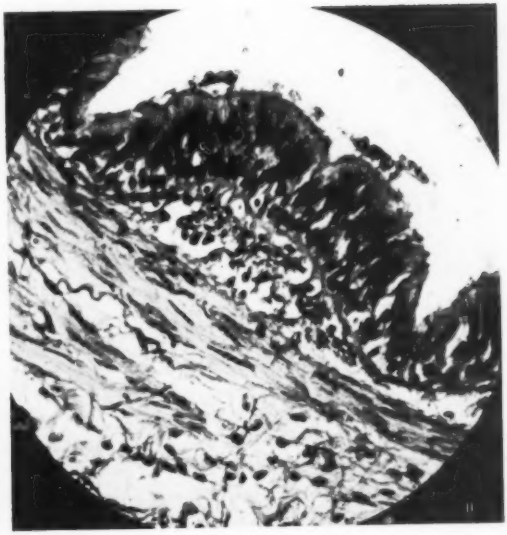

FIG. 11.—Fold of a small bronchus, stained van Gieson and Weigerts elastica. The interior of the fold is occupied by loose tunica propria-tissue and cross-cut elastic fibres. The basement membrane is well marked (×225).

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THE USE OF RADIOACTIVE PHOSPHORUS IN THE DIAGNOSIS OF PLEURAL EFFUSIONS

By A. J. Taylor, J. D. Pearson and N. Veall

From Southampton Chest Hospital and Physics Department, Guys Hospital Medical School, London, S.E.1

Experiments using radioactive phosphorus have shown that rapidly developing normal tissues, tissues undergoing acute inflammation, and neoplasms, take up relatively large amounts of phosphorus when it is given intravenously, and have a higher retention capacity for it than normal tissues (Kohman and Rusch, 1941; Jones, Chaikoff and Lawrence, 1941; Marshak, 1949).

On this basis Bauer, Moss and Richardson (1954) gave radioactive phosphorus intravenously and measured the concentration in pleural fluid at twenty-four hours in an attempt to differentiate pleural effusions of varying ætiology. They found that their cases fell into three groups—chronic effusions, acute inflammatory effusions and neoplastic effusions.

The figures quoted did not conclusively demonstrate that the test was a useful diagnostic measure. The main problem in diagnosis is to differentiate malignant effusions from those due to tuberculosis and pulmonary infarction; only one tuberculous effusion and three due to pulmonary infarction were included in the series. Even so the results seemed sufficiently promising and it was decided to carry out the examination in a larger number of cases.

Method

The method used was similar to that described by Bauer, Moss and Richardson (1954). Specimens were removed twenty-four hours after the intravenous injection of 100-200 microcuries of radioactive phosphorus and the ^{32}P content of the pleural fluid was compared with that of the plasma, using a liquid sample β counter (Veall, 1948).

Material

Fifty patients were examined in this way, all voluntarily, knowing that a small amount of radioactive material was being used. Eighteen of them had so-called malignant effusions, 8 had acute and 3 chronic tuberculous effusions, 5 effusions followed spontaneous pneumothorax, 3 were due to non-specific inflammation, 2 followed pulmonary infarction, 1 was a case of Meig's syndrome and 10 have remained undiagnosed.

Of the malignant group, only 2 were females and both had metastases from carcinoma of the breast. Of the acute tuberculous group, 6 were males and 2

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females. There was, as was to be expected, a discrepancy in the mean ages of these two groups, that of the former being 57 and of the latter 29.

Results

The results are summarised and the figures reported by Bauer, Moss and Richardson are given in Table I.

Table I.—Summary of the Results of the Radioactive Phosphorus Test on 39 Patients

Type of effusion	*No. of patients*	*Average Fluid % plasma*	*Range*
Malignant	18	81·0	25-123
Acute tuberculous	8	51·9	36- 83
Chronic tuberculous	3	77·3	54-113
Non-specific inflammatory	3	65·7	49- 85
Following pulmonary infarction	2	54·5	44- 65
Meig's syndrome	1	—	52
Following spontaneous pneumothorax ..	5	77·2	63-100
Results reported by Bauer, Moss and Richardson (1954)			
Carcinoma	16	79	28-150
Infarction	3	60	56- 63
Inflammatory	5	39	20- 52
Acute tuberculous	1	42	—

There is a statistically significant difference between the malignant and acute tuberculous groups (P=less than 0·01), but even so there is some overlap. The difference between the spontaneous pneumothorax and chronic tuberculous groups on the one hand and the acute tuberculous groups on the other is possibly significant (P=0·05-0·1). There is no significant difference between the malignant and the other groups except the acute tuberculous one.

Discussion

In the malignant group only 4 patients gave figures less than 75 per cent. One was a female of 35 with metastases from carcinoma of the breast who had had a course of deep X-ray therapy, and it was suggested by Bauer, Moss and Richardson (1954) that fibrosis following deep X-ray might explain the two unusually low figures (28 and 42 per cent.) in their series of 16 malignant effusions. The second lowest figure in this series was 37 per cent. and that was obtained in a man whose effusion was presumably caused by lymphangitis carcinomatosa from a primary gastric carcinoma; at a post-mortem examination his pleural membranes appeared quite normal. There was nothing unusual about the 2 patients from whom figures of 53 and 54 per cent. were obtained.

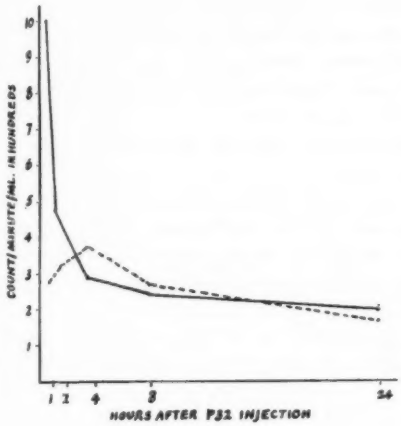

FIG. 1.

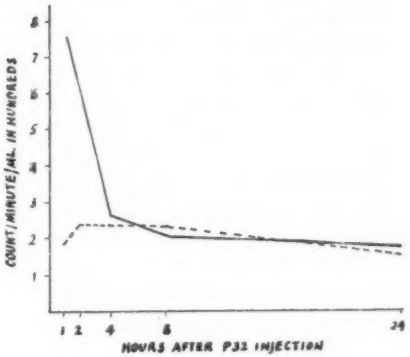

FIG. 2.

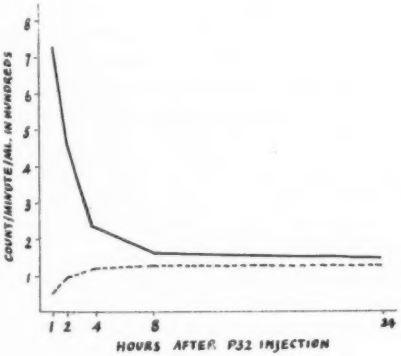

FIG. 3.

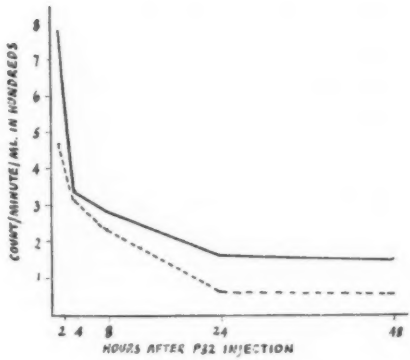

FIG. 4.

FIGS. 1, 2, and 3.—Radioactivity of serum and cell-free pleural fluid after intravenous injection of approximately 100 microcuries of radioactive phosphorus in three males with bronchial carcinoma and secondary involvement of the pleura.

FIG. 4.—In a 39-year-old male with an acute tuberculous effusion.

Only one acute tuberculous effusion gave a figure greater than 75 per cent. and that was in a man of 45 with an acute effusion of recent onset, but with radiographic evidence of previous disease in his upper lobe on the side of the effusion.

The patients in the chronic tuberculous group all had thickened pleural membranes, and those with effusions following spontaneous pneumothorax had all been treated with a pleural irritant possibly producing fibrinous deposits on the pleura and thickening of the pleural membranes.

The ratio in the case of Meig's syndrome, where one would expect the pleura to be virtually normal, was 52 per cent.

The reason for the difference between the acute tuberculous and malignant groups has not been explained. The high ratio in the malignant group might conceivably be due to a specific effect from malignant tissue, but that is unlikely because of a similar ratio in the chronic tuberculous, post-spontaneous pneumothorax and nonspecific inflammatory groups.

The difference in the figures is much more likely to be due to a difference in the ionic interchange between the blood and pleural fluid, related to the state of the pleural membrane.

This hypothesis tends to be supported by the results of serial estimations at intervals up to forty-eight hours after injection of ^{32}P. These results are presented in the form of graphs (Figs. 1-4). Figs. 1-3 are from patients with malignant effusions. The radioactive material seems to pass into the pleural fluid gradually, equilibrium being reached in from three to eight hours, with a steady falling off in radioactivity thereafter, due presumably partly to excretion and partly to redistribution in the various tissues of the body.

The graph (Fig. 4) from the only patient with an acute tuberculous effusion who was willing to submit to several thoracenteses for this purpose indicates that the radioactive material has passed into the pleural fluid relatively quickly, as if there was an easy communication between the blood and pleural fluid, with a rapid reduction in the radioactivity of both fluids up to twenty-four hours.

The radioactivity of the "acid soluble" and "acid insoluble" ("acid soluble" is material soluble in 10 per cent. trichloracetic acid (T.C.A.) and "acid in-

TABLE II.—THE DISTRIBUTION OF RADIOACTIVITY IN PLASMA AND PLEURAL FLUID TWENTY-FOUR HOURS AFTER INTRAVENOUS INJECTION OF RADIOACTIVE ORTHOPHOSPHATE

Type of effusion	*Fraction*
Malignant	Plasma "Acid Soluble" 75 cpm. Plasma "Acid Insoluble" 105 cpm. Fluid "Acid Soluble" 137 cpm. Fluid "Acid Insoluble" 4 cpm.
Following spontaneous pneumothorax	Plasma "Acid Soluble" 130 cpm. Plasma "Acid Insoluble" 160 cpm. Fluid "Acid Soluble" 120 cpm. Fluid "Acid Insoluble" 9 cpm.

soluble" is material insoluble in 10 per cent. T.C.A. and washed twice with it) fractions, of pleural fluid and serum after 32P injection, has been estimated in two patients, one with a malignant effusion and one following a spontaneous pneumothorax. The results are shown in Table II. These figures show that a considerable proportion of injected orthophosphate is firmly bound to "acid insoluble" material, presumably largely protein, in the plasma within twenty-four hours and that very little of that material has passed into the pleural fluid. The radioactivity of the pleural fluid, therefore, probably depends on the presence of phosphorus in, for the most part, inorganic compounds.

The total protein in acute inflammatory effusions tends to be relatively high and the alpha-2 globulin fraction in particular tends to be higher in these than in others (Taylor, 1958). The results in the radioactive phosphorus test may well depend on this and a modified Donnan membrane effect, but more detailed work would be required to provide a complete explanation.

Conclusion

When radioactive phosphorus in the form of orthophosphate is injected intravenously, the ratio

$$\frac{\text{cell free effusion fluid cpm.}}{\text{plasma cpm.}}$$

tends to be lower in acute tuberculous effusions than in effusions due to malignant disease. The reason for this is obscure. This finding is of limited value in differential diagnosis, and the test in its present form is not regarded as sufficiently specific to provide a diagnostic test for malignant effusions.

This article was part of a prize-winning essay in the 1957 South West Metropolitan Regional Hospital Board Clinical Research essay competition, and was part of a thesis accepted for the M.D. of Aberdeen University.

The authors would like to thank Dr. W. M. Macleod for permitting the investigations on his patients.

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THE VALUE OF SCALENE NODE BIOPSY IN INTRATHORACIC DISEASE

By H. C. Nohl

From the London Chest Hospital

"Les ganglions bronchiques sont comme le miroir du poumon," so spoke Parrot in 1876 in Paris on the relationship between the pathological changes in the lungs and those in the corresponding tracheo-bronchial lymph nodes. These lesions were constant and gave rise to "la loi des adenopathies similaires," or Parrot's Law.

Later Daniels (1949) showed that the lymph nodes, enmeshed in the deep cervial pad of fat overlying the scalenus anterior, reflected the pathological changes inside the thorax, and that a biopsy of these nodes could be of considerable diagnostic value. Many papers on "scalene node biopsy" have since been written (Shefts *et al.*, 1953; Harken *et al.*, 1954; Connar, 1955; Scott, 1957; Denk and Wurnig, 1957; Harvey and Harvey, 1958), but hardly any have been published in this country. Most of the authors are uncertain which side to select for exploration in the absence of palpable nodes. The object of this paper is to throw further light on this problem.

Shefts (1953) selects the right as the side of choice in cases of bilateral intrathoracic involvement because he considers it the safer procedure. In unilateral cases exploration of the same side as the intrathoracic lesion is advised. In the presence of bilateral mediastinal enlargement but absent pulmonary lesions he considers that positive nodes are most likely to be found on the left.

Both Harken *et al.* (1954) and Connar (1955) choose the side of exploration on the basis of the description of the lymphatic drainage of the lung by Rouvière (1932).

This author maintains that the lymphatic drainage of the lung does not confine itself to a lobar pattern and therefore divides both the right and left lung into an upper, middle and lower zone. The whole pulmonary lymphatic flow from the right lung goes to the right para-tracheal nodes. These nodes also receive the drainage of the left lower zone and the lower half of the left mid-zone via the subcarinal glands. The remaining portion of the left lung, he considers, drains upwards to the nodes in the left superior mediastinum.

Harken *et al.* (1954), therefore, advise that for right-sided lesions only the right scalene region need be explored. They carry out a bilateral procedure for lesions in the lower half of the left lung and a left scalene node biopsy alone for left upper lobe disease. Connar (1955) advises a bilateral exploration in addition for left mid-lung lesions. In patients with bilateral lesions or mediastinal mass and absent palpable supraclavicular nodes, he prefers a right-sided biopsy. Denk and Wurnig (1957), who investigated the incidence of scalene

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node metastases in 100 cases of bronchogenic carcinoma with no palpable nodes, advise a bilateral exploration.

The author's views on the pulmonary lymphatic drainage have been previously published (Nohl, 1956). The present study was largely carried out to examine still further the validity of the statements made in that paper, and also to record the experience with scalene node biopsy at the London Chest Hospital.

The Operation

The operative technique employed was similar to that described by Daniels, Harken and Connar. The operation requires care and operative skill: in one of the cases the internal jugular vein was injured, necessitating suture. This exploration is therefore best carried out under general anæsthesia, and particular caution is needed in the presence of superior vena caval obstruction. As the percentage of positive results depends on the extent and thoroughness of the exploration, especially in the absence of palpable lymph nodes, " keyhole surgery " must be condemned. A skin incision of 7-10 cm. in length is advised. Harken *et al.* (1954) explore even the upper mediastinum through this cervical approach and therefore prefer to call this operation " cervico-mediastinal exploration." The minimum extent of dissection is as follows: the area to be laid bare by removing all fat and its enmeshed lymph nodes is exposed by dissecting along the internal jugular vein downwards towards its junction with the subclavian vein. The upper border of this vein must be cleared. Laterally the removal of tissue is carried at least as far as the external jugular vein, but as there are often lymph nodes lying in the fat overlying the brachial plexus, there is no objection to dividing this vein and thus extending the dissection still further laterally. In the upper end of the wound the omohyoid will be exposed and can be retracted, so that excision can be achieved well above the upper border of this muscle. In this way the scalenus anterior with the phrenic nerve crossing it is laid bare, together with the transverse cervical and supra-scapular arteries. There should be no hesitation in dividing these vessels, if necessary, to effect a proper clearance.

Treatment of Biopsy Material

After operation it is advisable for the surgeon himself to remove all the lymph nodes, some of which are often not bigger than pinheads. This is best achieved with the bare fingers feeling for the different consistency of the lymph nodes in the surrounding fat. Once the whole block of tissue is hardened by formol-saline, it is not so easy to distinguish the glands from the fat, and recourse to multiple serial sections is necessary.

The histological sections are stained with haematoxylin and eosin, and in some cases where giant cells are seen Ziehl-Neelsen stains are necessary.

Results

Fifty-eight scalene node biopsies were done during the years 1954-58. In 41 cases there were palpable supraclavicular nodes, some of these were soft

and small and were missed at the first examination. In 17 cases no glands were palpable. Table 1 shows the incidence of positive biopsies in the cases with palpable nodes and in those where glands were not felt. In the latter group the preponderance of sarcoidosis is notable.

TABLE 1

	Total cases	*Positive scalene node biopsy*
Palpable nodes	41	36
Nodes impalpable	17	5 (4 cases sarcoidosis, 1 case bronchial carcinoma)

All the cases except three were ultimately diagnosed, if not by scalene node biopsy, then by bronchoscopy, pleural or lung biopsy, sputum cytology or by thoracotomy. Table 2 gives the final diagnosis of the whole series together with the number of positive scalene node biopsies. Two more diagnoses were made than there were cases, because each of two patients suffered from two diseases: one had Hodgkin's disease and a left upper lobe carcinoma, and the other had tuberculosis and a right lower lobe carcinoma. In each case the carcinoma was diagnosed by other means than scalene node biopsy. The other unexpected case was one with a supposedly left palpable supraclavicular gland, which turned out to be a small neurilemmoma. Scalene biopsy was particularly helpful in sarcoidosis, being positive in 8 out of 11 cases, if the 3 undiagnosed, but presumed sarcoidosis cases are included. This high incidence of positive findings with sarcoidosis has also been pointed out by other authors (Shefts, 1953; Carstensen, 1954; Connar, 1955; and Scott, 1957).

TABLE 2.—FIFTY-EIGHT CONSECUTIVE CASES OF SCALENE NODE BIOPSY

Diagnosis	*No. of cases*	*Positive biopsy*
Bronchogenic carcinoma:		
Squamous cell	6	3
Undifferentiated	11	8
Adenocarcinoma	5	4
Oat cell	4	3
Unspecified	11	5
Sarcoidosis	8	8
Reticulosis	1	1
Tuberculosis	2	2
Hodgkin's disease	3	2
Malignant pleural effusion (carc. breast, rad. mastect. 5 yrs. previous)	1	1
Hamman-Rich syndrome	1	—
Carcinoma of œsophagus	2	2
Carcinoma of stomach	1	1
Neurilemmoma (wrong clinical diagnosis)	1	1
Undiagnosed (probably sarcoidosis)	3	—
Total of diagnoses made	60	41

Table 3 gives the side of the chest lesion and the side of operation in the 41 cases in whom a positive biopsy was obtained. From it the following facts emerge. Right-sided lung lesions show pathological changes only in the right supraclavicular nodes. Disease in the left lung is much more often reflected in the right than in the left scalene nodes. When there is bilateral disease or bilateral hilar enlargement the right side is again more often involved. In both cases of œsophageal carcinoma the right supraclavicular nodes were infiltrated, while only the gastric carcinoma metastasised to the expected left side (signe de Troisier).

TABLE 3.—SIDE OF OPERATION ON WHICH A POSITIVE BIOPSY WAS OBTAINED AND THE SIDE OF THE CORRESPONDING LESION

Side of operation	*Left side*		*Right side*	
	Left	*Right*	*Left*	*Right*
Side of unilateral lung lesion	5	0	11	9
Centrally situated or bilateral lesions:				
Bilateral hilar enlargement		2		7
Normal chest X-ray		1		1
Bilateral reticulation		—		1
Carcinoma of the œsophagus		—		2
Carcinoma of the stomach		1		—
Neurilemmoma (wrong clinical diagnosis)		1		—
Total		10		31

Table 4 shows that even left upper lobe carcinomata give rise to metastases more often in the right than in the left supraclavicular nodes. Only one upper lobe growth metastasised to the left nodes; in the other case the left scalene glands were infiltrated by generalised Hodgkin's disease and not by the carcinoma.

TABLE 4.—SITUATION OF LEFT LUNG LESIONS WITH POSITIVE SCALENE NODE BIOPSIES

Situation of left lung lesion with positive scalene node biopsy on the right		*Situation of left lung lesion with positive scalene node biopsy on the left*	
Carcinoma of left main bronchus	2	Hodgkin's disease in scalene node and left upper lobe carcinoma	1
Carcinoma of left lower lobe bronchus	3	Carcinoma of left upper lobe bronchus	1
Carcinoma of left upper lobe bronchus	5	Carcinoma of left lower lobe bronchus	2
Carcinomatous mass in the left hilum	1	Left pleural effusion	1
Total	11	Total	5

Summary

The value of scalene node biopsy as a diagnostic procedure in intrathoracic disease is established beyond doubt. The percentage of positive biopsies depends on the thoroughness with which the operation is carried out and is especially high in cases of sarcoidosis. The results of the present study bear out the author's previously published views on the lymphatic drainage of the lungs and give a guide to the question of which side should be explored. Right-sided lesions always give rise to pathological changes on the right. In cases where no lymph nodes are palpable, the right supraclavicular region should be explored irrespective of whether the lesion in the chest is on the left or right. Similarly, in bilateral lesions a right scalene node biopsy is advised. Only when the left supraclavicular nodes are palpable should this side be operated upon. A bilateral exploration is only justifiable where a right scalene node biopsy is negative and the case cannot be diagnosed by any other means.

I would like to thank the medical staff of the London Chest Hospital for allowing me to use the case records of the patients under their care.

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PNEUMOCONIOSIS IN GRAIN WORKERS, OIL AND FLOUR MILLERS

By L. Dünner, R. Hardy, E. Nakielny, L. B. Robinson and G. A. Smart

From The Industrial Chest Diseases Clinic, Hull

References to pulmonary dust disease caused by the inhalation of vegetable dusts among those handling bulk cereals and seeds are scanty in the literature; most are from European countries other than the United Kingdom.

Kruger and Saupe (1928) described clinical and chest X-ray findings in 33 bakers and 25 millers; all had chest symptoms and X-rays showed either lung striations increased, reticulation, nodulation, or combinations of these, most marked in the millers. Jötten (1934) did not find any lung lesions due to grain-dust. Wohlhüter, Kleitz, Kraft and Mourot (1940) studied ten millers and bakers, in whom the chest condition, radiologically, was a nodular pneumoconiosis, in some progressing to massive fibrosis. Chemical analysis of five dust samples showed an average silica content (expressed as SiO_2) of 10-11 per cent. Heatley, Kahn and Rex (1944) reported the case of a wheat-loader whose chest X-ray showed bilateral reticulation and mottling. One of us (L.D.), jointly with Hermon and Bagnall (1946), published an account of pneumoconiotic lung changes in grain dockers in Hull; subsequent autopsy examinations of several men who died confirmed simple pneumoconiosis. Samples of grain dust were shown to have a content of 1-10 per cent. total silica, including up to 2·8 per cent. of soluble silicates. Stephanopoli de Comnène and Besson (1950) gave an account of pneumoconiosis in eighty-four silo-workers. Free silica, they found, was present in grain dust in amounts up to 0·6 per cent. The X-ray picture was of one of the three stages of pneumoconiosis, or a combination of two or more stages; in one case there was progressive massive fibrosis (P.M.F.). Asthmatic symptoms predominated in the group; sputum bacteriology revealed *Candida tropicalis* in a few. Autopsy studies showed the presence of sharp vegetable fibres and hairs, up to 35 μ in length, in the lungs, often compounded into structures like "asbestos-bodies," as found in asbestosis. The two authors exposed guinea-pigs to air-borne dust for nineteen days; when killed, these animals were shown to have acquired lung-damage—bronchiolitis obliterans, destructive changes in epithelial cells—and microscopic vegetable particles were found in the lung tissue. Dörr (1953) concluded that the fibrotic lung lesions resulted both from foreign body irritation, and from direct effects of the silica content of the cereal dust.

Rüttner and Stofer (1954) described one case of fibroblastic granulomatous reaction in lungs and intrathoracic lymph nodes, which they thought was due to inhaled particles setting up a cellular reaction; silica (absent from lungs in

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their case) was excluded as a factor contributing to lung fibrosis. Extensive interstitial pulmonary fibrosis was the autopsy finding of Gorincourt and Florentini (1954) in a case of grain-dust pneumoconiosis—a flour miller who, in life, had X-ray evidence of dense reticulation in both lungs. Chaumont (1955) recorded bilateral hilar adenitis in a young silo worker, that resolved in a few months. He did not exclude other possible ætiological causes of this condition. Trense (1955) found in a group of 120 grain loaders sharp, vegetable particles (0·01 to 3·5 mm. in length) in grain dust, of which the content of free silica varied from 1 to 9 per cent. Physical examination of dust analysed for free silica showed that nearly 80 per cent. was of particle-size (5-10), capable of invading the lung alveoli. Clinically, the group had symptoms of tracheo-bronchitis and emphysema; in 28, microscopy revealed sharp, needle-like particles in sputum, suggesting an " auto-cleansing " process on the part of the respiratory mucosa. Trense noted X-ray appearances of enlarged hilar shadows, reticulation, slight honeycombing, fine miliary nodulation, symmetrically distributed in lung fields. He regarded these changes as due to pneumoconiosis, but thought that the symptoms and disablement among the group were caused by bronchitis and emphysema rather than pneumoconiosis, which was radiologically not advanced.

Our series includes flour and oil millers, silo workers, grain workers, lighter and barge men, of whom the last four groups handle cereals and other seeds in bulk. Oil millers deal with non-cereal seeds and kernels of several varieties and carry out seed crushing, extraction of oils (*e.g.* linseed), and others that are later processed to become edible fats (margarine, cooking fats); the vegetable residues are made into cattle cake and poultry feed. Men in all these trades inhale vegetable dusts only. Grain dockers are excluded from the series as, in handling mixed cargoes, their work bears extra risk of inhaling mineral dusts (coal, pyrites, sulphur, etc). Hitherto we have been unable to observe men at work and have relied on descriptions of their conditions by workers themselves. These statements consistently described the bad atmospheric conditions, often in a narrowly restricted space, that used to obtain. For instance, when the bottom layer of grain in a ship's hold was shovelled into sacks, men could not see their work-mates similarly employed a few feet distant, but now better conditions prevail and grain from ship's hold, lighter or barge is moved directly into mill or silo by air propulsion or suction.

References to chemical analysis of grain dust done in Hull and elsewhere have been made earlier in this paper. Extraneous silica and silicates may be carried up from the soil by the growing plant. The Si atom, too, is a component of the vegetable molecule, replacing to some extent the C atom in such parts as the stem and seed envelope of the plant; the latter becomes the husk of the cereal when the plant matures and seeds ripen. Another potential source of silica in (or on) grain has been reported by Dr. L. Holzapfel, Director, Max Planck Institut für Silikatforschung in Berlin-Dahlem: in some exporting countries grain is sprayed with quartz powder before shipment to prevent growth of moulds, which may augment artificially the hazard of pneumoconiosis among grain workers.

Moulds and fungi flourish in flour and grain in conditions favourable to growth; their role, whether as infecting agents or allergens, in causing chest symptoms and contributing to disablement among our series, is unknown. Others have briefly referred to the finding, probably incidental, of fungi in the sputum of men in similar trades; these men were mostly either bakers or flour millers.

In the following description of 31 cases, no distinction is made between workers among grain and those handling non-cereal seeds; inhaling organic and siliceous dusts is common to both. All were first referred for investigation of chest symptoms, or were picked up on Mass Miniature Radiography examination, in which event they did not necessarily exhibit chest symptoms. For convenience, the series is headed by five cases which came to autopsy, confirming pneumoconiosis or dust-fibrosis in four. Although suspected in others on clinical, or radiological grounds, pneumoconiosis was not proven in the other 26, as autopsies were not carried out. In only six of the whole series were the X-ray appearances normal, showing no suggestive evidence of pneumoconiosis, or any other condition.

Chest X-ray and Morbid Anatomical Findings (5 Cases)

(1) G.E., 50 years, lighterman for thirty-eight years. X-ray: Marked striation; emphysema in the lower zones. Four years later bronchial carcinoma was found. P.M. Excessive dust and slight simple pneumoconiosis, emphysema. Squamous cell carcinoma and metastases in the hilar nodes. Histologically small zones of active tuberculosis were found in the lung and hilar nodes.

(2) H.C., 62 years, silo foreman (grain) for forty-four years. Recently small hæmoptysis. X-ray: Carcinoma in right middle zone; no manifestations of pneumoconiosis. Right pneumonectomy for carcinoma. Report on the specimen: there is only little dust and histologically very slight fibrosis around the dust deposit. The carcinoma is the squamous type. The pathologist did not find any dust that he could recognise as vegetable.

(3) F.W., 56 years, oil miller for forty years. For one year, severe dyspnœa and productive cough. X-ray: Fibrosis in right upper zone and left middle zone (Fig. 1). P.M. Histologically very extensive fibrosis. There is some excess dust in other parts of the lung. The bronchi are dilated and in the bronchial pus there are fungal colonies of the actinomyces type. The pathologist thought this should be regarded as secondary to and not the cause of, fibrosis.

(4) G.T., 43 years, oil miller for four years. For several years, cough and sputum; recurrent small hæmoptyses. X-ray: Several small nodules in left upper zone and a larger one above the right hilum. No radiological evidence of pneumoconiosis. Sputum positive for tubercle bacilli. Death after five years. P.M. Histologically the small foci of pneumoconiosis are identical with those seen in coal miners. Bronchitis, general emphysema, and active tuberculosis.

(5) G.P., 45 years, lighterman for twenty-one years. For 7 years, cough and sputum; asthma. Clinically: slight asthma and bronchitis. X-ray: Infiltration in both upper zones. Cavity in right upper zone. No manifestations of pneumoconiosis. Sputum always negative. P.M. Tuberculosis in both upper zones;

cavity in right upper zone. Fibrosis probably due to tuberculosis. No dust deposits. No evidence of pneumoconiosis.

Chest X-ray and Other Findings (26 Cases)

(6) A.G. 52 years, flour-miller for twenty-one years. For two years, cough, sputum and dyspnœa. X-ray: dense, coarse reticulation in both mid-zones and less in left upper zone. Thin-walled translucencies in both upper zones. Emphysema in both lower zones, especially left (Fig. 2).

(7) G.B., 51 years, oil miller for seven years. For several years, cough, sputum and severe dyspnœa. X-ray: prominence of left hilum. Some nodulation in left-lower zone, probably with some fibrosis. Several small nodules in right upper zone below the right clavicle. Emphysema in both lower zones and right mid-zone.

(8) A.P., 49 years, flour miller for eighteen years. For several years dyspnœa, gradually worsening. X-ray: reticulo-nodulation in both lower zones and left mid-zone (Fig. 3).

(9) H.S., 53 years, flour miller for thirty-eight years. Severe dyspnœa, loss of weight and small hæmoptyses for two years. X-ray: reticulation in right mid-zone, emphysema in left lower zone.

(10) E.H., 65 years. Working for about twenty years as a clerk in an oil mill where he was exposed to dust of seeds. Discovered by M.M.R. No symptoms. X-ray: fibrosis in right lower zone.

(11) J.A., 62 years, flour miller for thirty-eight years. Discovered by M.M.R. Only occasionally short of breath (due to age?) X-ray: reticulation in both lower zones. Emphysema in both upper zones. Round focus in left mid-zone at the level of the hilum.

(12) A.R., 47 years, lighterman for twenty-two years. Rather severe dyspnœa for several years. X-ray: reticulo-nodulation in right upper zone and emphysema in left lower zone.

(13) H.F., 57 years, oil miller for thirty-two years. Dyspnœa for one year. Œdema of the legs for one month. X-ray: marked striation, fine nodulation in right upper zone and coarse in left lower zone (Figs. 4, 5, 6).

(14) H.A., 68 years, bargeman for twenty-six years. Developed tuberculosis with positive sputum ten years before being seen at the Clinic. X-ray: At that time showed dense infiltration in right upper lobe, less in right mid-zone. No evidence of pneumoconiosis. Later, tuberculosis seems to have healed. Present X-ray: fibrosis in right upper zone. Large rounded focus in right mid-zone and a smaller one in right lower zone. No sputum available.

(15) W.C., 32 years, silo worker for eight years. Dyspnœa on exertion. Sputum positive for tubercle bacilli. X-ray: infiltration in both upper zones, especially the right. In the following ten years improvement of tuberculosis. Many sputum tests negative X-ray: several hard foci in right upper zone. Some fibrosis and suspected soft foci in right upper zone. Emphysema in right mid- and lower zone.

FIG. 1.—Case 3. Oil miller for forty years. X-ray chest showing fibrosis in the right upper and left mid zones.

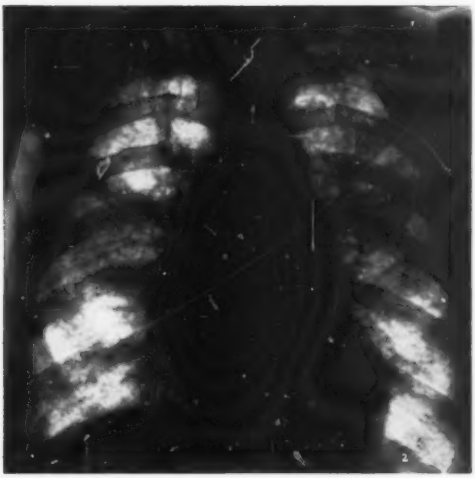

FIG. 2.—Case 6. Flour miller for twenty-one years. X-ray chest showing gross reticulation in both mid zones and the left upper zone.

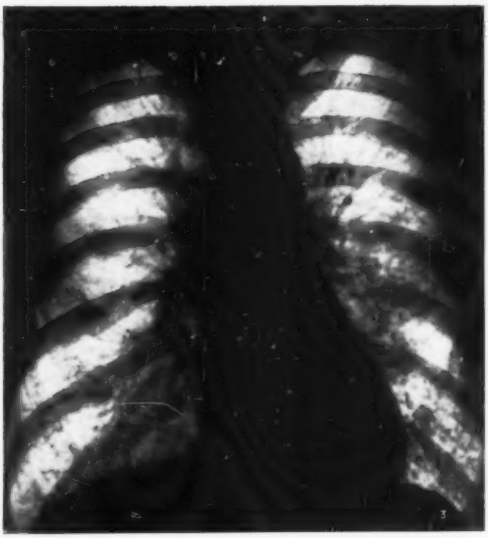

FIG. 3.—Case 8. Flour miller for thirty-eight years. X-ray chest showing reticulation in both lower zones and the left mid zone.

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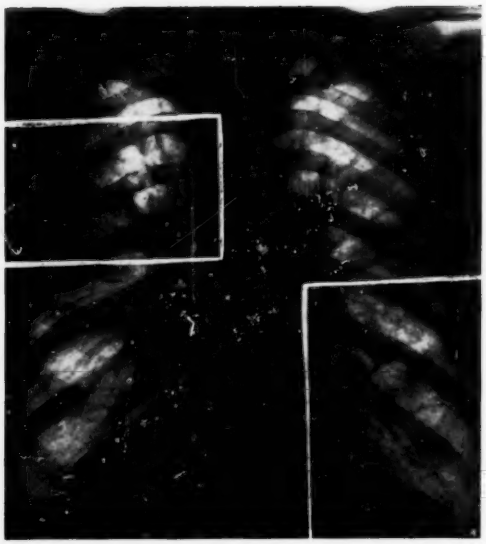

Fig. 4.

FIGS. 4, 5 and 6.—Oil miller for thirty-two years. X-ray chest showing increased striation and fine nodulation in the right upper zone (detailed in Fig. 5) and the left lower zone (detailed in FIG. 6).

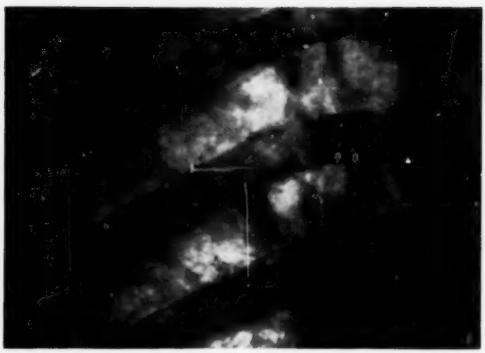

FIG. 5.

FIG. 6.

(16) G.S., 73 years, flour miller for twenty years. In mental hospital for psychosis. X-ray: diffuse, rather dense infiltration in left upper zone, to a lesser degree in right mid-lower zone. Discrete nodules in left lower zone. Sputum always negative for tubercle bacilli. Treatment with antibiotics for seven months. During the treatment sputum turned out to be positive for tubercle bacilli. X-ray (after eight months): considerable decrease of the infiltration in left upper zone and right mid-lower zone. Other manifestations seen on the second X-ray are either tuberculosis or pneumoconiosis. The appearances that resolved were definitely not pneumoconiotic, but due to tuberculosis or were unspecific.

(17) L.E., 61 years, lighterman for twenty-three years. Dyspnœa and pains in chest which gradually decreased. X-ray: coarse reticulation in both mid-zones, especially left.

(18) C.W., 34 years, lighterman for twenty years. Found by M.M.R. No complaints. X-ray: no definite manifestations.

(19) W.U., 53 years, silo-worker for thirty-three years. For many years dyspnœa and productive cough. X-ray: enlarged hilar shadows; reticulation in left mid-zone.

(20) W.T., 77 years, silo worker for thirty years. When 57 years old was found to have pulmonary tuberculosis with positive sputum, which became negative at 68 years of age. X-ray (when 77 years of age): Several hard, rounded, well-defined foci in right upper zone. Rather dense shadow in left upper zone, emphysema in left lower zone.

(21) T.S., 50 years, silo worker for twenty-one years. No complaints. X-ray: probably healed pulmonary tuberculosis in right upper zone.

(22) L.S., 34 years, lighterman for nine years. No complaints. X-ray: normal.

(23) G.L., 47 years, oil miller for thirty-three years. No complaints. X-ray: old apical tuberculosis; slight reticulation in left mid-zone.

(24) C.L., 64 years, bargeman for fifty years. For many years, cough and sputum; for three years severe dyspnœa. Recent hæmoptysis. X-ray: mottling in both lower zones.

(25) G.I., 64 years, oil miller for forty-seven years. Acute pain in the chest due to right spontaneous pneumothorax. X-ray: Right pneumothorax with fluid level which subsequently resolved completely. Later X-ray: normal.

(26) M.H., 40 years (female), flour packer for six years. No complaints. X-ray: normal.

(27) E.C., 40 years, oil miller (cattle food) for six years. "Always" cough and sputum. For several days, blood-stained sputum. X-ray: normal.

(28) W.C., 41 years, oil miller for sixteen years. Occasionally dyspnœa. X-ray: marked striation slight nodulation in left lower zone.

(29) C.F., 50 years, bargeman for thirty-two years. For many years cough

and sputum. For two years dyspnœa. X-ray: retraction of heart and mediastinum to the right.

(30) J.A., 57 years, flour miller for thirty-three years. Dyspnœa. X-ray: normal.

(31) J.A., 55 years. silo-worker for seven years. Recently severe dyspnœa gradually increasing. X-ray: calcification in right upper zone. Both hilar slightly enlarged.

Signs

Physical signs in the chest, as in other pneumoconioses, are not diagnostic and were seldom helpful even in advanced lung damage or when there was complicating disease such as tuberculosis or new growth.

Sputum

Apart from the finding of tubercle bacilli in 3 cases, specific bacteria and fungi were absent, and vegetable particles or fibres were not detected, in contrast with the reported findings of others.

X-ray Appearances

The main patterns were (*a*) normal (or nearly) lungs, (*b*) general increase in lung striation, (*c*) fine or coarse reticulo-nodulation, (*d*) irregular, patchy fibrosis, (*e*) general or localised emphysema, (*f*) small, rounded foci, either tuberculomatous or pneumoconiotic. Progressive massive fibrosis (P.M.F.) was not seen. Six of the series had normal X-rays.

Similar patterns are recognised in other types of pneumoconioses, so that we feel justified in accepting them when they occurred either singly or in combination as presumptive evidence of pneumoconiosis. In case 3 the type of fibrosis differs from the nodular fibrosis of silicosis (the term " fibrosis " is reserved by some to describe silicotic nodulation and P.M.F. only), but, in the absence of a past history of pneumonia, lung abscess, or other acute chest illness, we attribute it to the effects of dust inhalation for long periods, and have found similar lesions revealed by X-raying and later confirmed at autopsy in other groups of pneumoconiosis. It is certain that, where chest disability and dyspnoea are present in these workers, it is due in part to emphysema, which is often progressive. Emphysema of one or more of the following types is a common autopsy finding in the several groups of occupational lung disease studied by us in Hull (Dünner, 1957). Clinical and/or X-ray evidence of it may have been absent during life: (1) General. (2) Compensatory. (3) Focal (always associated with simple pneumoconiosis. (4) Localized. (5) Sub-pleural emphysematous bullæ.

Emphysema may be clinically obvious or be indicated by pulmonary function tests. It should be suspected when there is discrepancy between the grade of dyspnœa and the absence or paucity of radiological lesions. Straight X-ray (or tomography) may reveal some of these types of emphysema, but this evidence is often lacking.

Morbid Anatomical Findings

In occupational lung disease, morbid anatomical findings are decisive whatever the X-ray evidence. Of the five who came to autopsy, only one (case 5) showed no evidence of dust disease. Irregular, often extensive fibrosis, as in case 3, has been found in other pneumoconioses but we have not felt justified in calling it "pneumoconiosis" in the accepted sense.

Pathogenic fungi, incriminated by some workers as a cause of fibrosis, were absent except in one case (3) where actinomyces was found in bronchial secretions at post-mortem, the pathologist regarding the fungus as saprophytic. Unlike some other workers, we have been unable to detect either in the lung discharges during life, or in the tissues post mortem, any vegetable particles or fibres.

Pulmonary tuberculosis was found in 10 cases of the series; in 3, tubercle bacilli were peresent in sputum; 4 had X-ray evidence during life of inactive or healed tuberculosis; 3 others were shown to have active pulmonary tuberculosis at post-mortem. Definite conclusions cannot, of course, be drawn about the incidence of tuberculosis in this industrial group, of which our series is only a small, selected sub-group. On the other hand, we found (Dünner and Hardy, 1951) an apparently high incidence in grain dockers—75 cases in a series of 192, of whom 54 had "open" pulmonary tuberculosis. The evidence seems to suggest however, that chronic exposure at work to inhaling irritant organic dust is a predisposing factor. Bronchogenic carcinoma was diagnosed during the lifetime of two of our series. In one (case 1) post-mortem examination confirmed the diagnosis and showed also the presence of simple pneumoconiosis and active tuberculosis. In the other (case 2), pneumonectomy was done, subsequent examination showing histologically little dust fibrosis and squamous-celled carcinoma.

Summary

Chest disease and morbidity has been studied among a group of 31 persons (grain workers, oil and flour millers, flour packer) exposed to inhaling mixed vegetable dusts at work. Pulmonary fibrotic lesions or simple pneumoconiosis were found histologically in 4 out of 5 cases in which post-mortem examination was done. Radiologically, various types of lung damage (reticulation, micronodulation, irregular fibrosis) were encountered, conforming with the histological findings in 4 out of the 5 cases in which we were able to obtain post-mortem examination. Emphysema associated with this and other types of occupational lung disease has been discussed, and 10 cases of tuberculosis and 2 of bronchogenic carcinoma have been noted. Only in six cases were chest appearances normal.

We wish to express thanks to Prof. J. Gough, Cardiff, for histological examination of the lungs, and his valuable help, and also to Dr. A. P. Massie, Consultant Pathologist, Hull.

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PLASMA CELL TUMOUR OF TRACHEA

By I. W. B. Grant and J. D. Ross

From the Northern General and Royal Victoria Hospitals, Edinburgh, and the Department of Tuberculosis and Diseases of the Respiratory System, University of Edinburgh

Primary tumours of the trachea are rare. Ellman and Whittaker (1949) concluded from a detailed survey of the literature that carcinoma formed the largest single group (37 per cent.), followed in order of frequency by cartilaginous tumours, papilloma, sarcoma and fibroma. Other types of primary tracheal tumour occasionally reported include adenoma, mixed (salivary) tumour, lipoma, lymphoma, rhabdomyoma, angioma, endothelioma and so-called amyloid tumour. The trachea may also be the site of an extra-medullary plasma cell tumour or plasmacytoma, a new case of which is reported here.

Case Report

Male, aged 45 years; railway worker.

The patient first came under our observation in March 1955, following an attack of acute bronchitis. During childhood he had suffered from frequent illnesses diagnosed as pneumonia and for many years had had the symptoms of chronic bronchitis and emphysema with productive cough, wheeze and breathlessness on exertion. In 1939 the patient was admitted to a tuberculosis hospital following the discovery of bilateral pulmonary fibrosis in the chest radiograph. He was in hospital for three months and during this time acid-fast bacilli were reported in two sputum smears. Numerous subsequent examinations have, however, been negative for tubercle bacilli on film and culture.

For about fifteen years the patient had experienced recurring dysphagia, and because it was thought that the pulmonary changes might be related to this he was admitted to the Royal Victoria Hospital in May 1955 for further investigation. The clinical picture on admission was predominantly that of chronic bronchitis and emphysema. The sputum was scanty but mucopurulent. Slight cyanosis and early finger clubbing were present. On examination of the chest there were scattered rhonchi and numerous basal crepitations, particularly on the left side.

The chest radiograph showed diffuse streaky markings with fibrotic changes most pronounced in the upper half of the right lung field and in the left lower zone, where the appearances suggested partial lower lobar collapse; cystic translucencies due to bronchiectasis were distinguishable in the right parahilar area. Barium swallow showed abnormal muscular spasm and inco-ordination at the upper end of the œsophagus with an appearance suggesting an " œsophageal web." Some barium passed into the trachea. Bronchography demonstrated extensive bronchiectasis involving all lobes of the right lung, the left lower lobe and the lingula, as well as the diffuse changes of chronic bronchitis. In the lower half of the trachea three discrete, rounded, smooth filling defects were seen, the diameter of the two largest being just over 1 cm. (Fig. 1).

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The patient refused bronchoscopy and œsophagoscopy at this stage, but dysphagia persisted and he eventually agreed to œsophagoscopy in February 1956. No abnormality was observed at this examination, but it was followed by complete relief of the dysphagia.

In February 1957 he was readmitted with an acute exacerbation of bronchitis which responded satisfactorily to treatment with penicillin and antispasmodics. On this occasion he consented to bronchoscopic examination.

Bronchoscopic Findings. The larynx was normal. Two tumours were observed on the tracheal wall. The more proximal arose from the left lateral wall of the trachea 7·5 cm. below the vocal cords and 6 cm. above the main carina. It was a sessile, slightly lobulated tumour with an intact glistening epithelial surface. The base of the tumour measured 1·5 cm. and it projected 1 cm. into the tracheal lumen. The second tumour was quite separate from the first, being situated 2 cm. distally with its upper surface 4 cm. above the level of the main carina. It was more pedunculated and slightly larger than the other tumour, measuring 1·5 by 1·5 cm., but was otherwise similar in appearance. Both tumours were firm but not hard and did not bleed when touched with the sucker. Tissue was taken from the distal tumour for histological examination. The main carina and all right and left bronchi were normal.

Histological Report on the Tracheal Tumour (Dr. N. Maclean). "No respiratory epithelium or tracheal glands are included in the specimen. The tissue is composed of a solid sheet of plasma cells supported by fibrous stroma (Fig. 2). The plasma cells are large and are frequently binucleate. Their nuclei, although rather hyperchromatic, are fairly mature and no mitotic divisions are observed. The appearance of the plasma cells, their arrangement and the absence of other inflammatory cells suggest that this tissue is neoplastic.

Conclusion: Plasma cell tumour involving trachea."

No evidence of diffuse myeloma was found on further investigation, which included examination of the peripheral blood and sternal marrow, chemical analysis of the urine and tests of renal function, estimations of the serum proteins (including electrophoresis), the serum alkaline phosphatase and serum calcium, and radiographs of the skeleton. The erythrocyte sedimentation rate was 13 mm. at one hour. The serological reactions for syphilis were negative. On examination of the nasal cavity, nasopharynx and pharynx no other tumours were found and there was no enlargement of the cervical lymphatic glands.

At this stage treatment with X-rays or urethane was considered but rejected, as it was felt that the potential improvement in the tracheal airway did not warrant exposing the patient to the discomfort and risks of these forms of treatment.

He was discharged from hospital in May 1957 and continued at work until November 1957, when he was admitted as an emergency to a medical unit in another hospital. He was collapsed, cyanosed and almost moribund and was considered to be suffering from influenzal bronchopneumonia. He recovered from this episode and was able to return home, but his chronic respiratory symptoms had increased in severity. Dyspnœa and tightness in the chest forced him to rest after walking less than 100 yards on the flat, and his wife reported episodes of cyanosis and mental confusion. He was, therefore, readmitted to the Royal Victoria Hospital in December 1957 for reassessment.

The bronchographic and bronchoscopic findings were unchanged. Full investigation again showed no evidence of diffuse myeloma. The vital capacity

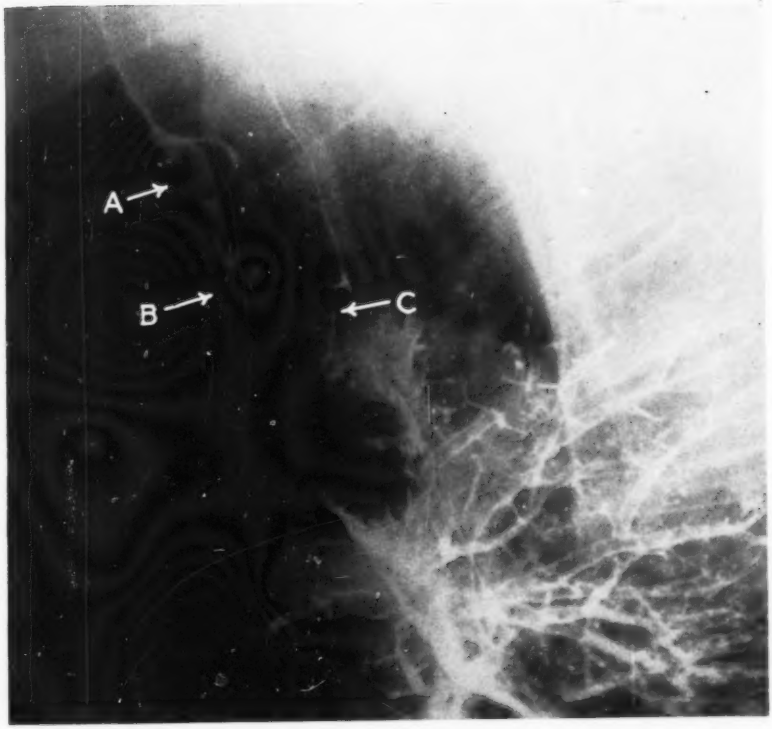

FIG. 1.—Lateral radiograph showing three tracheal tumours outlined by opaque medium. Tumours A and C were visible on endoscopy, but tumour B was concealed by tumour A.

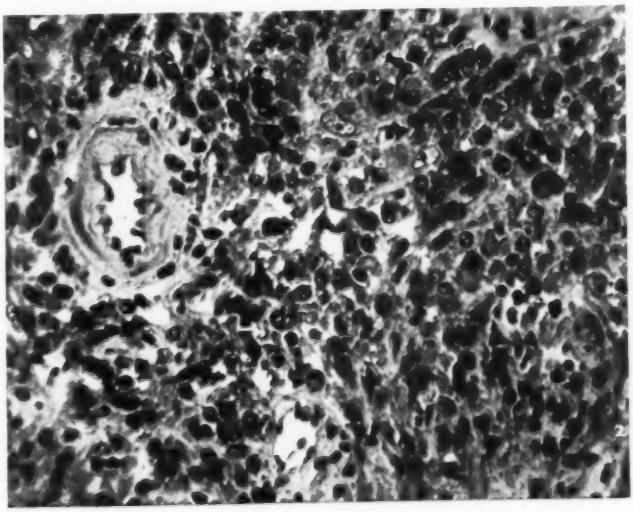

FIG. 2.—Photomicrograph (×450) of tracheal tumour composed entirely of plasma cells.

To face p. 300

was 1,050 ml. (predicted 3,000 ml.) and the forced expiratory volume (2 sec.) was only 720 ml. Insignificant improvement in these figures was obtained after an intravenous injection of aminophylline 0·5 g. An electrocardiogram was consistent with cor pulmonale.

In view of the grave impairment of respiratory function now accompanied by anoxæmia and cor pulmonale it was decided to irradiate the tracheal tumours in the hope of improving pulmonary ventilation and alleviating symptoms.

In February 1958 radiotherapy was given to the tracheal region with the 4 Me V linear accelerator to a total dosage of 4,000 rads. over a period of two weeks. He was also given tetracycline 0·25 g. four times daily on a long-term basis in an effort to control respiratory infection.

When his condition was reassessed in May 1958 he claimed a slight improvement in his breathlessness, but his clinical state was, in fact, unchanged. No improvement was recorded in ventilatory function tests and the arterial oxygen saturation at rest was reduced to 91·7 per cent. Bronchoscopic examination showed no change in the size or appearance of the tracheal tumours.

Discussion

Extra-medullary plasma cell tumours may occur in association with diffuse myeloma or may arise as primary lesions in soft tissues. In diffuse myeloma necropsy studies have shown that the organs most commonly involved are liver and spleen, followed in diminishing order of frequency by lymph nodes, kidney and lung. Extra-medullary lesions were found in 27 (71 per cent.) of 38 cases of diffuse myeloma reported by Hayes, Bennett and Heck (1952) and in 22 (73 per cent.) of 30 cases reported by Churg and Gordon (1950).

Primary extra-medullary plasma cell tumours differ in their anatomical distribution from those found in association with diffuse myeloma. They most commonly arise in the upper respiratory passages or in the oral cavity. According to Dolin and Dewar (1956) these were the sites of origin of the tumour in 126 (78·1 per cent.) of the 161 cases reported up to 1956, and it has been estimated (Jaeger, 1941) that 0·5 per cent. of all new growths of the upper air passages are plasma cell tumours. In the other 35 cases almost every organ in the body, except the brain, was included among the sites of origin, the highest figures being for stomach (7) and ileum (5). Eighty per cent. of cases occurred in males, mostly between the ages of 40 and 70 years.

When the primary tumour presents in the upper respiratory passages or in the oral cavity it is usually a pale pink, firm, round or lobulated mass at least 1 cm. in diameter, either pedunculated or polypoid. Microscopically it consists almost exclusively of plasma cells arranged in clusters or sheets, with a scanty connective tissue stroma. It is important to distinguish the true plasma cell tumour from the so-called plasma cell granuloma, but this seldom presents serious difficulty as in the granuloma other cells, such as polymorphonuclear leucocytes, lymphocytes and fibroblasts, are invariably present in addition to plasma cells. Caution is required, however, in accepting a diagnosis of plasma cell tumour of the conjunctiva as this condition may be confused with trachoma. The plasma cell tumour is usually single, but may be multiple

(about 10 per cent.). It may invade adjacent tissues, including bone, *e.g.* skull in the case of nasal or naso-pharyngeal tumours. Usually invasion occurs slowly, but occasionally the process is rapidly progressive. Metastatic involvement of regional lymph nodes, observed in about 25 per cent. of cases, does not carry unduly grave implications, as many of these patients survive in relatively good health for several years. Some patients, probably about 10 per cent., develop metastatic deposits in other organs, most commonly in bones. With multiple bone involvement the condition may become indistinguishable from diffuse myeloma. This development may occur within a few months of the appearance of the primary extra-medullary lesion or may be delayed for several years. Only when bone involvement occurs are the characteristic biochemical change of diffuse myeloma found in patients with extramedullary plasma cell tumours.

Localised tumours in a favourable situation for surgical treatment can be excised, and some lesions may respond, even dramatically, to radiotherapy. With both forms of treatment, however, recurrence is common and the prognosis in general is poor, 50 per cent. of patients dying within four years of diagnosis. The outlook is slightly better when the primary tumour is situated elsewhere than in the upper respiratory tract or the oral cavity.

Only six plasma cell tumours involving the trachea have previously been described. In the case reported by Heindl (1933) the primary lesion was a single large mass in the naso-pharynx. This was successfully excised, but three years later two similar tumours developed in the trachea and two more in the right main bronchus. Kreibig (1933) reported a case in which a plasma cell tumour was found simultaneously in the conjunctiva and the trachea. Both were excised, but the tracheal tumour recurred nine months later. Ellinger (1936) reported a double plasma cell tumour in the middle third of the trachea in a patient presenting with symptoms of respiratory obstruction. The case report was illustrated by a reproduction of a radiograph showing the tumours outlined by opaque medium. In the case reported by Hinz (1941) the tumour arose in the left main bronchus close to its origin and not in the trachea itself. That reported by Jaeger (1941) originated in the sub-glottic region of the larynx and involved only the upper end of the trachea. In the most recently recorded case (Mathieson, 1956) the tumour was situated at the upper end of the trachea. The patient, a man aged 18, who had presented with breathlessness and stridor of a year's duration, was admitted to hospital with what was regarded as status asthmaticus and died five days later. Necropsy revealed a lobulated tumour $2 \times 2 \times 1{\cdot}5$ cm., projecting from the left lateral tracheal wall 1 cm. below the vocal cords. On histological examination it was a typical plasma cell tumour. Death was due to respiratory obstruction complicated by pneumonia.

In the case reported in this paper the following are the most noteworthy features:

(1) The tumour was multiple but confined to the trachea.

(2) The reduction of the tracheal lumen was not considered to be responsible for the patient's symptoms.

(3) The lesions were discovered accidentally when bronchography was carried out for an apparently unrelated condition.

(4) The diagnosis of plasma cell tumour was made by bronchoscopic examination and tracheal biopsy.

(5) The tumours were not observed to increase in size during a period of almost three years, and were subsequently not influenced by radiotherapy.

Summary

A case of primary plasma cell tumour of the trachea is reported in a man with extensive bilateral bronchiectasis, chronic bronchitis and emphysema. The tracheal lesion was multiple, but there was no evidence either of metastatic spread to the regional lymphatic glands or of diffuse myeloma.

The literature on extra-medullary plasma cell tumours is briefly reviewed with special reference to tracheal involvement.

Our thanks are due to Dr. N. Maclean for the histological report, to Professor R. McWhirter and Dr. J. Newall for advice and administration of radiotherapy, to Dr. A. C. Douglas for his help in the preparation of this paper, and to the Royal Victoria Hospital Tuberculosis Trust for providing secretarial assistance.

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FAMILIAL PULMONARY EMBOLISM

By N. F. Crofts

From Keycol Hospital, Sittingbourne, Kent

Although pulmonary embolism is a common condition causing 2 to 3 per cent. of all deaths in hospital (Brooks, 1952), it is rare for it to affect several closely related persons.

Wright (1952) mentions that he has studied several families with thrombosing tendencies, and describes the case of a woman of 54 who had a pulmonary embolism following bilateral femoral thrombosis.

She had seven close relatives who suffered from thrombosing conditions, including five pulmonary embolisms. Investigations failed to reveal a significant common factor.

The chief purpose of this report is to describe a case of pulmonary embolism in a young man with an unusual family history of that condition. It is thought that familial pulmonary embolism has not previously been described in the British medical literature.

Case Report

A man of 28, a physics and chemistry laboratory technician, developed right-sided pleural pain and fever on 1.12.57. The pain ceased after one week but the pyrexia continued. On 7.12.57 his family doctor began treatment with erythromycin 0·5 g. four-hourly, and this was continued for two days until his admission to hospital. There was no past history of serious illness and no family history of tuberculosis.

Physical Examination on Admission

He was a well-built, slightly obese man. His temperature was 102° F. (38·9° C.) and the pulse rate was 100, but he appeared to be comfortable and did not complain of any symptoms apart from a slight unproductive cough which had been present for only two days.

The percussion note was dull and crepitations were heard over the base of the right lung posteriorly. There were no other abnormal signs. The blood pressure was 150/80.

Investigations

Urine normal. Mantoux 1.T.U. positive.

Blood count: Hæmoglobin 97% (14·2 g./100 ml.). White cells 4,000/mm. Polymorphs 83%. Eosinophils 2%. Lymphocytes 13%. Monocytes 2%.

E.S.R. 60 mm. in one hour.

Acid-fast bacilli were not found in the three specimens of sputum examined.

Serum complement fixation tests were negative for influenza A, B and C,

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the A.P.C. group of viruses, Q fever and psittacosis. The agglutination test for streptococcus M.G. was also negative.

A chest radiograph showed a small collection of fluid in the right costophrenic angle but otherwise was normal.

250 ml. of blood-stained fluid were aspirated from the right pleural cavity. It contained numerous eosinophils, a few polymorphs and lymphocytes, but no organisms were seen or cultured.

Treatment and Progress

Crystalline penicillin, 1 million units intramuscularly eight-hourly, was given for five days starting on 12.12.57, but appeared to have no effect on the fever or clinical condition.

On 17.12.57 fluoroscopy showed that a small pleural effusion had formed on the left side. The effusion on the right was unchanged. Two days later treatment with streptomycin 1 g. intramuscularly daily, PAS 6 g. twice daily and INAH 150 mg. twice daily was begun, as it seemed possible, though not probable, that the patient was suffering from acute tuberculous pleurisy. The pyrexia was not affected by this treatment, the temperature remaining between 100° and 102° F.

In the early morning of 21.12.57 he died suddenly.

Necropsy Report (Dr. J. L. Dales)

External. The body was that of a well-built young man. Apart from pallor there was no external evidence of disease.

Internal. The pleural cavities contained about 1 pint each of bloody fluid. The lower lobes of both lungs were lightly adherent to the chest wall and diaphragm. Both lower lobes showed oldish infarcts and the left lung showed infarction of the upper lobe as well. The branches of the pulmonary veins were filled with thrombus. In addition there was a very recent large thrombus in the main right pulmonary artery.

Both common iliac veins contained fragmentary thrombus lightly adherent to the vein walls. The femoral veins were free from thrombus. The liver, spleen and kidneys were congested.

Post-mortem Diagnosis

Pulmonary infarction.
Pulmonary embolism.
Thrombosis of the common iliac veins.

Family History

After the necropsy it was learned that four close relatives had suffered from pulmonary embolism.

The patient's father, an obese man of 52, died in 1955. He was admitted to hospital with the diagnosis of coronary thrombosis. At necropsy massive thrombus was blocking the main branches of the pulmonary artery, recent infarcts were found in both lungs and a large ante-mortem thrombus was present in the right femoral vein. There was no evidence of coronary artery disease.

The father's sister was admitted to hospital as an emergency case in 1947

at the age of 39. Five weeks previously she had had a normal delivery. Symptoms due to bilateral pulmonary infarcts occurred shortly before admission and several days later both thighs became swollen. Thrombosed veins were palpable in the thighs. The uterus was fully involuted. There was radiological evidence of consolidation at the base of the right lung. She was treated with penicillin and discharged well five weeks after admission.

Her son, a cousin of the patient, was admitted to hospital in 1956 at the age of 18 with an infarct at the base of the left lung due to thrombo-phlebitis of the left calf. He was treated with anti-coagulants for three weeks and then discharged. Two months later he was readmitted with a recurrence of thrombophlebitis in the left leg.

Investigation results were as follows:

Blood count, hæmoglobin 113%=(16·7 g./100 ml.).
White cells, 6,350/c.mm.
Polymorphs, 66%.
Lymphocytes, 28%.
Monocytes, 6%.
Platelets, 250,000/c.mm.
Prothrombin time, 13 seconds (control 13 seconds).
Prothrombin content, 100% of normal.
Bleeding time, 1·5 minutes (Duke's method).
Clotting time, 4 minutes (Lee and White's method).

He was treated again with anti-coagulants and later discharged on sulphadiazine 1 g. daily, which he continued to take for over a year. He remains well.

The father's brother died of pulmonary embolism at the age of 21 about thirty years ago. No hospital records are available.

The patient was an only child. There was no history of thrombosis on the mother's side of the family.

Discussion

Coincidence is unlikely to account for the frequency of pulmonary embolism in this family because of the age at which three of its members were affected—18, 21 and 28 years respectively. Pulmonary embolism is rare in young people unless there is some obvious precipitating cause such as a surgical operation or heart failure. None of these patients had any such condition and it therefore seems highly probable that they had inherited some factor predisposing to pulmonary embolism. What this factor might be is not known. It might be an increase in blood coagulability, but if that were so it is surprising that none of the four patients had a history of other thrombosing conditions. States of increased coagulability cannot be identified with certainty by any known laboratory test or combination of tests, and it is likely that any changes which may occur in the platelets or clotting mechanism in such cases are transitory.

Another suggestion is that these patients inherited some anatomical abnormality which led to slowing of the venous circulation in the legs and pelvis. No such condition was found in the two who came to necropsy.

It is now realised that unheralded pulmonary embolism is not very rare.

Cohen and Daley (1957) record ten cases, eight of whom appeared to be fit and active up to the time of the embolism. However, only one of their patients, a woman of 21, was less than 38 years old.

In the case of the patient who is the subject of this paper, pulmonary infarction was considered as a possible cause of his pleural effusions, but was rejected on the grounds that it was most unlikely to occur in an apparently fit and active young man, especially as there were no symptoms or signs of venous thrombosis.

He therefore unfortunately did not receive anti-coagulant treatment.

Summary

A case of pulmonary embolism in a young man is described.

The high incidence of this condition in his family is discussed.

I wish to thank Dr. Owen Clarke and Dr. John Lipscomb for permitting me to describe cases under their care and for their encouragement.

I am also grateful to Dr. J. L. Dales for his necropsy report.

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ADVANCES IN THE PHARMACOLOGICAL STUDY OF CERASE—A NEW ANTI-TUBERCULOUS AGENT

By Mahmoud Kamal Muftic

Royal Hospital, Basrah, Iraq

Cerase was first described in 1906 by Metalnikov as a hypothetical enzyme, which decomposes waxy membranes of *Mycobacterium tuberculosis*. This enzyme was present in crude extracts of whole larvæ of the wax moth (*Galleria mellonella*). In spite of years of research the enzyme has not yet been isolated in a pure state. Besides Metalnikov and his collaborators in the Pasteur Institute (Paris), attempts to isolate such enzymes were carried out by Dublet (1921), Kuzniecow and Wojciechowsky (1950), Niemierko (1950) and Mankiewicz (1949 and 1952). The first bacterial cerase was isolated in 1945 by Muftic from cultures of *Blastomyces cerolytica*, a yeast-like fungus which utilises waxes and wax-like substance as its sole carbohydrate source. Further purification (Muftic, 1951, 1952) allowed parenteral administration of cerase, which has a strong anti-mycobacterial action *in vitro* and *in vivo*. The first human cases of tuberculosis treated with it were described by Thaller, Rojc-Marchesi and Muftic. Crystalline cerase having been prepared (Muftic, 1955), investigation of its properties was continued, and it was shown to be an iron containing enzyme with peroxidase action on saturated paraffin bonds. Crystalline cerase contains C, H, N, O, P and Fe. Details of its solubility, stability and standardisation have been reported elsewhere (Muftic, 1957).

Antimicrobial Activity

Cerase is not an antibiotic. It is a constitutional enzyme present in different micro-organisms and insects, representing a part of their digestive system. It does not interfere with the metabolism of mycobacteria, except in so far as it changes osmotic conditions on cell membranes by oxidising and decomposing wax-like substances. Mankiewicz (1952) has demonstrated progressive abolition of acid-fastness in *Mycobacterium tuberculosis* ($H_{37}Rv$) after treatment with cerase obtained from wax-moth larvæ. The reduction of acid fastness was proportional to the concentration of enzyme and the time of contact. Muftic (1955) observed peroxide formation in the cell wall of *Mycobacterium tuberculosis* treated with dilute cerase solution. In experimental tuberculosis of guinea-pigs cerase exerts a strong protective effect in comparison with control animals. About ½ gramme of cerase protects a guinea-pig from 1 mg. of moist culture of *Mycobacterium tuberculosis* $H_{37}Rv$ (Muftic, 1956). In the table is shown the antimicrobial spectrum of cerase, obtained from *Blastomyces cerolytica*. It seems to lyse only acid-fast microbes, attacking only Mycobacteria

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ANTIMICROBIAL SPECTRUM OF CERASE

Micro-organism	*Minimal antimicrobial concentration µg./ml./hrs.*
Aerobacter aerogenes	—
Actinomyces israeli	80
Bacillus subtilis	—
Brucella bronchiseptica	—
Clostridium perfringens	—
Corynebacterium diphtheriæ	—
Criptococcus neoformans	—
Diplococcus pneumoniæ	—
Endamœba histolytica	—
Escherichia coli	—
Micrococcus aureus	—
Mycobacterium smegmatis	3
Mycobacterium phlei	3
Mycobacterium tuberc. Valle R_1	2
Mycobacterium tuberc. $H_{37}Rv$	2
Neisseria gonorrhœæ	—
Penicillium roqueforti	—
Proteus vulgaris	—
Pseudomonas aeruginosa	—
Salmonella typhosa	—
Sarcina lutea	—
Saccharomyces cerevisiæ	—
Serratia marcescens	—
Shigella dysenteriæ	—
Streptococcus viridans	—
Staphylococcus albus	—
Trychophtyon rubrum	—

and Actinomycetaceæ. Other micro-organisms, Gram-positive and Gram-negative bacteria, fungi and protozoa are not affected.

PHARMACOLOGY

According to Thaller and Muftic cerase has very little acute and chronic toxicity. They found that it is well tolerated by mice, guinea-pigs, rats, cats, pigeons, rabbits, dogs and human beings. Muftic (1946) found that cerase has an LD_{50} in guinea-pigs of 1,500-1,800 mg. per kg. of body weight. Death is due to anaphylactic shock. Dogs which received daily intravenous injections of 100 mg. per kg. of cerase for twenty weeks tolerated the enzyme well, and such treatment did not alter the cellular elements of the blood nor the blood non-protein nitrogen. No evidence of nerve damage was demonstrated in cats following intramuscular administration of cerase at a level of 200 mg. per kg. for twenty weeks. Preliminary reports indicate that cerase causes few side effects in human beings when administered intramuscularly or intravenously. Intramuscular injections cause slight local pain.

ABSORPTION AND EXCRETION

Following intramuscular injection in rabbits (200 mg. per kg.) the enzyme can be detected in the blood after four hours. The peak concentration is reached

after thirty-eight hours, equivalent to peroxidasic activity of 3-6 μg. per ml. of whole blood. This concentration is maintained for forty-eight hours and then a very slow decline begins. Complete disappearance of peroxidasic activity after a single injection of 200 mg. per kg. (rabbit) takes five weeks. As the peroxidasic value is not a sensitive method for the detection of cerase, however, no definite conclusion has yet been reached as regards its elimination from the body. Intravenous administration of doses of 100 mg. per kg. cause similar blood concentrations in rabbits, but the concentration falls rapidly from the peak after five hours. After intravenous administration less than 4 per cent. of the total peroxidase activity is demonstrable. This very low concentration seems to reflect the rapid uptake of the enzyme by different tissues. Cerase is not absorbed by blood cells, as shown by lack of activity of cells separated from defibrinated blood to which the enzyme is added. After intramuscular or intravenous administration in rabbits the enzyme is not detectable in the urine. After oral administration of various doses blood and urine samples show no peroxidase activity. This is so whether the cerase is given in capsule form or in an acid-resistant coated tablet.

Protective and Therapeutic Effect

The protective action of wax-moth cerase in tuberculous guinea-pigs was demonstrated by Metalnikov (1941, 1920), Mankiewicz (1952) and Muftic (1956). According to Muftic a total dose of 0·5 g. of fungal crystalline cerase protected guinea-pigs infected intraperitoneally with $H_{37}Rv$. The suppression of infection was evident in comparison with control animals. They usually died 19 to 60 days after infection, whereas cerase-treated animals killed 140 days after infection showed histological healing of lesions.

Few data are available concerning human cases treated with cerase; they include two necropsy reports of patients who died from hyperpyrexia. Tubercle bacilli were not isolated from either. The other data comprise records of 6 patients treated ten years ago, 7 cases four years after treatment, and 37 patients treated from three years to one year ago. Such limited clinical material was not sufficient for proper therapeutic evaluation of cerase, but some conclusions can be drawn. The enzyme was given in doses of 30-50 mg. per kg. of body weight, injections being given intramuscularly and intravenously at various intervals from five to fourteen days. In all cases a quick disappearance of acid-fast bacilli from sputum, laryngeal swabs and stomach washings was observed. A decrease in E.S.R. and radiological improvement of diseased lungs were also noted.

Allergic Reactions

Cerase (from *Blastomyces cerolytica*) is an iron protein. Its molecular weight is probably 235,000. Parenteral administration of such a foreign protein would be expected to cause sensitisation, with the formation of specific antibody and the probability of anaphylactic reactions. However, such reactions have in fact only been observed, either in animals or human beings, when large doses were

given as mentioned earlier. Temporary urticaria was observed in three human subjects; reactions related to the Arthus or Schwartzman phenomena were not seen following intramuscular or intravenous injection. Following the first dose of cerase in some tuberculous animals and humans hyperpyrexia developed. This was seen only in tuberculous cases; normal animals and human beings tolerate the enzyme without any elevation of body temperature. After three to four doses in the tuberculous animal or man hyperpyrexia no longer occurred, suggesting that this reaction is a response to sudden tuberculinisation of the body consequent upon lysis of tubercle bacilli by cerase. Bacteria-free filtrates of *Mycobacterium tuberculosis* exposed to cerase contain a pyrogen, probably similar to tuberculin.

Clinical and Necropsy Findings

The post-therapeutic follow-up period for human cases treated by cerase varied from one to ten years. All patients became sputum negative within 14-60 days of the first cerase injection. They showed marked clinical improvement, cavities no longer being visible on repeated X-ray examination, including tomography. Out of 56 treated cases 39 have resumed regular activity. Two cases died from hyperpyrexia, but during the first week of treatment their sputum became negative. At autopsy deep jaundice without peripheral œdema, and fleshy enlarged lymphatic glands, were found. The liver was enlarged and its cut surface showed fine infiltration. The bile ducts were patent and the gall bladder, apart from a few concretions, was normal. The spleen was enlarged and soft with small pale areas scattered through its substance. In the abdomen there were grossly enlarged glands, the architecture of which had been destroyed. Microscopic examination of the enlarged glands showed caseous tuberculosis, with much necrosis, fibrosis and prominent giant cell formation. No tubercle bacilli were demonstrated. The sternal marrow showed an intense eosinophilia with paucity of normoblast cells. Death probably occurred from hepatic failure caused by tuberculous involvement of the liver, precipitated by sudden tuberculinisation and hyperpyrexia. These cases demonstrate the close relationship between cerase administration and its pyrogenic properties, and the violent reaction of a hypersensitive organism induced by sudden lysis of mycobacteria and release of tuberculins or tuberculin-like substances.

Summary

Although several enzymes have previously been tried therapeutically, cerase is the first to show definite antibacterial effect. Low toxicity and highly specific antibacterial activity facilitate clinical research, and the apparent anti-tuberculous activity in both animal and human cases justifies larger scale clinical trials, which are in progress. Besides bibliographical data, this article contains information about the pharmacological properties of cerase, and preliminary observations on its use in the treatment of human tuberculosis.

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EFFECT OF ADEQUATE LONG-TERM CHEMOTHERAPY ON RELAPSE IN PULMONARY TUBERCULOSIS*

By A. C. Ronald and J. F. Stitt

From Toronto Hospital, Weston, Ontario

Experience of long-term chemotherapy in pulmonary tuberculosis has been accumulated for several years. It is now becoming possible to review large groups of patients who have been treated under relatively standard conditions and to form an opinion regarding the efficacy of such treatment.

In this paper we have attempted to review those patients with pulmonary tuberculosis who were discharged from the Toronto Hospital, Weston, by medical consent during a period of two and a half years, ending June 1956, after having received what was then considered " adequate chemotherapy." At least two but more commonly all three of the standard drugs, namely PAS, isoniazid and streptomycin, were used. The duration of treatment was at least one year, but there were a very few exceptions in patients with minimal disease who were discharged before one full year of treatment was completed. Surgical procedures were undertaken when indicated and formed part of the accepted treatment régime.

Unlike most other reports in the literature,[1,2] this paper deals only with patients discharged under the conditions outlined above. It is not an attempt to review the fate of all patients with pulmonary tuberculosis admitted during the time in question. It ignores the fact that there were some treatment failures and some deaths in sanatorium, to say nothing of irregular discharges; it is not a detailed statistical analysis of a therapeutic trial carefully planned in advance, but a retrospective report of the results of adequate treatment.

Material and Methods

The records of all patients discharged from this hospital between January 1, 1954, and June 30, 1956, were considered. These numbered 1,734 and from these patients with pulmonary tuberculosis satisfying our criteria of adequate treatment were selected for retrospective follow-up study. Of 850 considered suitable, 648 were actually traced by direct questionnaire, reports from their family doctors or routine reports from municipal and other chest clinics. The shortest time of follow-up was two years, the longest four and a half years.

We have excluded patients with tuberculous pleural effusion and those who had primary disease; six patients died of causes other than tuberculosis. Of the 648 patients studied, 298 were males and 350 were females. The age distribution and extent of the disease at the time of admission are shown in Table I.

* Based on a lecture given at Canadian Tuberculosis Association in Quebec, June 12, 1958.

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TABLE I.—AGE DISTRIBUTION AND EXTENT OF DISEASE AT TIME OF ADMISSION

All cases	*Min.*	*Mod.*	*Far*	*Bacil.*	*Age*	
					Under 40	*Over 40*
648	191	285	172	531	451	197

When patients were first admitted, three 24-hour and three 72-hour specimens of sputum were examined by concentration and culture for tubercle bacilli. When sputum could not be obtained, three samples of fasting gastric contents were cultured. By these methods, of the 850 patients, 680 (80 per cent.) were found to be positive.

TREATMENT

All patients under present review received chemotherapy. Streptomycin, PAS and isoniazid were given concurrently in most cases. Forty-seven patients received only two drugs, usually because they could not be desensitised satisfactorily or because their tubercle bacilli were known to be resistant to one or other of the three drugs. The average dose of isoniazid was 300 mg. daily and of NA. PAS 14 g. daily. Streptomycin was given at a dosage of 1 g. twice weekly. We believe that any danger of drug resistance involved in giving streptomycin intermittently is more than compensated by the simultaneous use of PAS and isoniazid daily.

As already stated, chemotherapy in sanatorium was of at least one year's duration, but was much longer in some instances. Only a very few patients with minimal disease were permitted to leave after a stay of less than one year, and only if continuing co-operative and supervised chemotherapy was reasonably certain. The average approved duration of stay in sanatorium was 18·5 months in 1954, 15·3 months in 1955, and 12 months in 1956.

The patients' progress was reviewed at definite intervals and when necessary surgical treatment was advised and undertaken. Thoracoplasty was performed in 21 patients (3 per cent.), almost all of these in 1954. Major resection (lobectomy or pneumonectomy) in 45 cases (6·9 per cent.) and minor resection (wedge or segmental resection) in 61 (9 per cent.).

* N.T.A. Classification (1957).

Minimal—Slight lesions without demonstrated excavation confined to a small part of one or both lungs. The total extent of the lesions, regardless of distribution, shall not exceed the equivalent of the volume of lung tissue which lies above the second chondrosternal junction and the spine of the fourth or body of the fifth thoracic vertebra on one side.

Moderately advanced—One or both lungs may be involved, but the total extent of the lesions shall not exceed the following limits.

Slight disseminated lesions which may extend through not more than the volume of one lung or the equivalent in both lungs.

Dense and confluent lesions which may extend through not more than the equivalent of one-third the volume of one lung.

Total diameter of cavities less than 4 cm.

Far advanced—Lesions more extensive than moderately advanced.

Relapses

Relapse occurred in 20 cases (3·1 per cent.), during our follow-up studies. In addition 5 patients were re-admitted to this or other hospitals for recurrence of pulmonary symptoms, which, however, could not be attributed to reactivation of pulmonary tuberculosis. We feel reasonably certain that all patients who re-entered hospital have come to our attention because of the system of notification in force in this country and the high standard in which records are maintained at this hospital.

Table II shows the nature of the relapse, whether clinical, bacteriological or radiological, and the time elapsed since discharge.

Table II.—Type of Relapse and Time Interval

Total No. cases	*Type of relapse*			*Time interval*		
	Clin.	*Bact.*	*Radiolog.*	*0-1 yr.*	*1-2 yr.*	*2 yr. or more*
20[1]	11[2]	9	14	7	9	4

[1] One case developed tuberculous lymph glands but showed no new pulmonary disease.
[2] Five cases were re-admitted with pulmonary symptoms but no evidence of reactivation of tuberculosis.

It includes the 5 patients who were re-admitted because of active pulmonary disease, in whom reactivation of tuberculosis could not be confirmed. With the exception of 4 cases, all relapses occurred within two years; 7 occurred in the first year. One relapse case died three months after discharge and death was registered as due to pulmonary tuberculosis. However, no autopsy was performed. Another case developed tuberculous cervical adenitis with no reactivation of her pulmonary lesion.

In the process of selecting suitable cases for follow-up, those patients in whom resistance to more than one drug was discovered were discarded from our series. In non-bacillary cases this could not be determined. Amongst the 20 relapse cases, 18 had been bacillary and Table III indicates the drug sensitivities at commencement of treatment.

Table III.—Bacteriology and Drug Sensitivity at Commencement of "Adequate" Treatment

Total No. cases	*Bact.*	*SENSITIVITY STATUS*		
		Unknown	*Fully sens.*	*Part. resis.*
20	18	5	11	4

In 15 this is known, and of these 11 had organisms fully sensitive to all the drugs. In 4 partial resistance to one drug was found. Sensitivity was not recorded in 3 of the bacillary cases because of technical difficulties with the

sub-cultures, but the fact that rapid sputum conversion occurred suggests that the organisms were fully sensitive.

Age appeared to be a contributing factor; 5·5 per cent. of those over the age of 40 and 2 per cent. of those under that age relapsed. Similarly, as might be expected, the relapse rate was higher in males (4 per cent.) than in females (2·3 per cent.). This is shown in Table IV, which also indicates in some detail the treatment received by these relapse patients as well as the extent of the disease at the time of the first adequate course of therapy.

TABLE IV

	Sex		*Age*		*Extent of disease*				*Strep. PAS*	*Strep. INH*	*Strep. PAS*	*Maj.*	*Min.*	*Thoro.*
	Male	*Female*	*Under 40*	*Over 40*	*Min.*	*Mod.*	*Far*	*Cavity*						
"Follow-up group" ..	298	350	451	197	191	285	172	—	601		47	45	61	21
"First treatment" relapse cases	5	5	5	5	2[1]	5	3	6	8	0	2	0	0	1
With treatment prior to first "adequate course" ..	7	3	4	6	0	5	5	8	8	1	1	1	0	2

Of the 20 patients, 14 had cavitation and in 8 the disease was far advanced. In 10 the disease was classified as moderately advanced. In these cases minimal treatment time was thirteen months, the maximum thirty months. Three patients had thoracoplasty and 1 had a lobectomy with decortication. The 10 cases who had treatment prior to their "adequate" course of therapy are further considered in Table V.

TABLE V.—RELAPSE CASES WITH TREATMENT PRIOR TO "ADEQUATE" CHEMOTHERAPY

No previous sanatorium admissions	*No. pts.*	*Previous inad. chemotherapy 2 drugs 3-6 mo.*	*SURGERY*		*Bed rest only*
			Pneumothorax		
1	6	4	1	0	2
2	4	2	0	2	0

Six had one previous admission and 4 had two previous admissions. Six had one or more short courses of chemotherapy and 2 had bed rest only. Thoracoplasty had been performed in two patients.

Discussion

The percentage of patients admitted to sanatorium with active tuberculosis who are successfully treated and subsequently discharged as inactive has risen steadily since antibiotic treatment was first introduced. This favourable situation can be directly attributed to the effectiveness of chemotherapy and the greater use of surgical resection made possible by it.

Tuberculosis is a chronic disease with a marked tendency to recur, and not enough is known about the efficacy of prolonged chemotherapy in maintaining this state of inactivity after treatment has been discontinued. One might

well wonder to what extent chemotherapy brings about a more permanent cure than older methods of treatment. Enough time has now elapsed for reasonably prolonged follow-up studies and several reports have recently appeared in the literature.[1, 2, 3] Most of these, however, are detailed statistical analyses of the fate of all patients after admission to treatment centres, whereas we have confined ourselves to the study of those discharged, sputum negative, after successful treatment of at least one year's duration. This again contrasts with other reports where treatment was usually shorter by quite a considerable amount, or dealt with groups of patients in whom only a certain proportion received the amount of therapy we here call adequate. In the pre-antibiotic era, the relapse rate varied from 10 to 20 per cent. for minimal disease to 40 per cent. in far advanced disease. The relapse rate in our series is 3·1 per cent. Undoubtedly relapses will continue to recur in this group over the years; however, it is known that the majority of relapses occur within the first two or three years after discharge and it is therefore not unreasonable to expect that this will be the case with our group. We would conclude from this study that the relapse rate in pulmonary tuberculosis has been considerably reduced by the use of long-term chemotherapy, plus surgical treatment in those cases where it is indicated. It is apparent, too, that relapse is most likely to occur in patients with some degree of caseation or other irreversible changes remaining after prolonged chemotherapy. This is not surprising, since most of these lesions contain viable tubercle bacilli and, because of their potentiality for reactivation, form a constant source of danger to the patient. Amongst our 20 cases that relapsed, there were 4 in whom resection was recommended but not performed for various reasons, and 4 more in whom resection was not possible because of age or extent of disease. Only 1 patient in whom a resection was performed has relapsed to date.

Other factors contributing to relapse were alcoholism, and partial gastrectomy which had been performed in 2 of those numbered amongst the relapses.

One patient had silicosis in addition to his tuberculosis and 1 patient was pregnant at the time relapse was detected. In only 1 patient were we unable to find even a tentative reason for his relapse; he was a young man aged 22 who had fifteen months of three-drug therapy and who followed medical advice in every respect, yet relapsed clinically and radiologically and again became sputum positive.

The present status of the relapse cases may be of some interest. Ten cases were re-treated and are considered satisfactory. Six are still being treated, of which only one is not doing well. One patient was discharged with open-negative disease as maximum benefit. One patient died. Two patients are being observed by other doctors, having refused re-admission.

Our ideas on the duration of chemotherapy have not altered much since 1956. The total is rarely less than eighteen months, even for minimal disease. The length of hospital stay, however, is becoming less, as has already been indicated by the averages of approved length of stay. Patients with minimal disease, for example, are discharged after nine months as a rule. Resection is

considered an important part of treatment, being undertaken in those cases where residual caseous foci or cavities remain after six to nine months of adequate chemotherapy.

Summary

This paper is a review of patients with pulmonary tuberculosis at the Toronto Hospital, Weston, " adequately " treated and discharged by medical consent between January 1954 and June 1956. It is not an account of a study carefully planned in advance, but a retrospective report of results obtained by treatment then in vogue (namely long-term chemotherapy with at least two drugs, but usually three, for a period of one year, and surgical measures where these seemed to be indicated).

The total number of all patients discharged during this time was 1,734. Of these, 850 were considered suitable for review in that they satisfied our criteria of adequate treatment. Six hundred and forty-eight were actually traced and of these 20 have relapsed to date (June 1958); 5 more were readmitted because of recurrence of symptoms of pulmonary disease, but reactivation could not be established; 6 patients died of causes other than tuberculosis. The relapse rate is thus 3·1 per cent.

The relapse cases were studied in detail. The ages ranged from 22 to 67 years and 10 of the 20 patients were aged 40 years or less at time of relapse. Eight were females and 12 were male patients.

Sensitivity to drugs was complete in 11, unreported in 3, and in 2 patients tubercle bacilli were not cultured. Partial resistance only to one drug was encountered in the remaining 4 patients. Only one of the 20 patients had a resection (lobectomy) performed, but 3 had thoracoplasty as part of their treatment before relapse. It is of interest that in 4 patients resection was considered necessary but was not done for various reasons.

This study seems to confirm tentative conclusions previously held by us regarding predisposition to relapse after treatment.

We should like to thank Dr. C. A. Wicks for facilities placed at our disposal.

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THE FUTURE OF THORACOPLASTY IN PULMONARY TUBERCULOSIS

By Deirdre M. Drew and James O'Rourke

From St. Mary's Chest Hospital, Dublin

In the past ten years rest and collapse therapy have been superseded by chemotherapy and resection as the principal measures in the treatment of tuberculosis. Thoracoplasty is still used more than pneumothorax, but resection has become the operation of choice for many surgeons " in the hope of a quicker and more comfortable result " (Sweet, 1946). Resection has belied its theoretical disadvantages and there has been no sudden deterioration in results as the years of follow-up increase. In few centres has enthusiasm for Medlar's dictum prevailed—excision of all residual foci whenever possible—but persistent cavities and blocked cavities are still viewed uneasily, even in the presence of a negative sputum, and these suspicions, to many, are best resolved by removal. There are cases, however, where thoracoplasty is feasible and resection is not. To deny thoracoplasty any place in treatment, even of patients with extensive bilateral disease, is at least premature. We propose in this paper not to discuss thoracoplasty versus resection, for, as Cleland (1957) has remarked: " the very fact that thoracoplasty, or its modifications, is employed as an alternative to resection where the latter is contra-indicated means that it is never really

Table I

	A	*B*	*C*	*D*	*All cases*
Number	31	101	96	218	446
	%	%	%	%	%
" Operative mortality "	12·9	3	2·1	0·5	2·2
Died later	12·9	0	1	2·3	2·2
Alive, unsatisfactory	9·7	3	9·4	1·8	4·3
Satisfactory after ipse-lateral excision	9·7	3	9·4	3·2	4·9
Satisfactory without ipse-lateral excision	51·6	89·1	74	84·4	80·9
Lost sight of	3·2	2	4·2	7·8	5·4

A = Patients sputum positive within three months before the first stage who received a year's or more chemotherapy in the two pre-operative years.

B = Patients sputum negative for three months at least before the first stage who received a year's or more chemotherapy in the two pre-operative years.

C = Patients sputum positive within three months before the first stage who received less than a year's chemotherapy in the two pre-operative years.

D = Patients sputum negative for three months at least before the first stage who received less than a year's chemotherapy in the two pre-operative years.

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legitimate to compare the results of the two forms of treatment except where such cases can be regarded as truly comparable." It seems more useful to consider the results of thoracoplasty in the light of present circumstances, when drugs are so effective and patients older: to assume that thoracoplasty may still be performed and to indicate what results may be expected.

Material

Four hundred and forty-six patients had thoracoplasty carried out for pulmonary tuberculosis at St. Mary's Chest Hospital in the years 1951-56 inclusive: apart, that is, from thoracoplasty for empyema without active lung disease or as a planned preliminary to resection, and from correctoplasty. The earlier cases at St. Mary's—82 patients operated on between August 1949 and the end of 1950—were reviewed by Flanagan (1955). In his series 7 (8·5 per cent.) died; 11 (13·4 per cent.) were lost sight of; 42 (51·2 per cent.) had completely satisfactory results. Eight (9·8 per cent.) had sporadic positive cultures more than two years from their final stage, but were otherwise well; 8 (9·8 per cent.) had relapsed.

In the present series, 24 patients (5·4 per cent.) have been lost sight of. Among the remainder, followed 1-7 years, 20 (4·5 per cent. of the total) are dead, the operative mortality—within three months—accounting for half that figure. Twenty-two (4·9 per cent.) are satisfactory after partial resection or pneumonectomy under the thoracoplasty. Three hundred and sixty one (80·9 per cent.) are satisfactory without any further ipse-lateral surgery than revision thoracoplasty in two cases. Four of these 361 required subsequent contralateral surgery (plombage; extra pleural pneumothorax) or A.P. (2 cases). In 2 other cases active contralateral disease settled without any special treatment at all. In 5 patients (1·1 per cent.) thoracoplasty appears to have controlled the underlying disease, but the other lung, 2-5½ years post-operatively, shows evidence of active tuberculosis.

Among those lost sight of, 19 (79·1 per cent.; 4·3 per cent. of the total) were well when last seen and had suffered no complications.

We have regarded patients who are sputum negative, radiologically stable and free from any significant disability arising from their chest condition as "satisfactory." However, only 261 of the 361 (58·5 per cent. of the total) have been entirely free from operative or later complications. Eight patients have had minor hæmoptysis but are otherwise well; the bleeding has come from underlying bronchiectasis. In 5 others extrapulmonary tuberculosis manifested itself—cervical adenitis, renal disease, bone involvement—but is no longer active. Sixteen have had respiratory illnesses—asthma, non-tuberculous pneumonitis, bronchitis—or complain of productive cough or some dyspnœa on exertion. One patient was diagnosed as suffering from cardiac failure after a confinement but is well twelve months later. Another three have chest pain that is not incapacitating; two are anæmic and two in poor general condition without any particular symptoms. Two had post-operative "spreads" evidently from the operation side, which cleared on chemotherapy: in 6, the contralateral disease worsened but later settled on drugs. In 14 other patients

now satisfactory the only complications were post-operative: wound sepsis, space infections, hæmothorax, axillary thrombosis, marked bronchospasm.

In the earlier years covered by the series it happened not uncommonly that the sputum remained positive for a considerable time after operation: 32 patients were positive more than three months after the final stage, but later converted without any further treatment other than, in 7 cases, chemotherapy. All these had less than twelve months' chemotherapy in the two years before thoracoplasty.

Sex Side

Two hundred and fifty two of the patients were female, 194 male. 80·1 per cent. and 82 per cent. respectively are known to be satisfactory, without ipselateral resection. In 226 the thoracoplasty (or initial thoracoplasty in any bilateral case) was on the left side (80·5 per cent. satisfactory): in 220 on the right (81·8 per cent.).

Failures

Twenty patients (4·5 per cent.) are dead. Ten died at operation or within three months, 9 in direct consequence of the surgery and 1 from a previously unsuspected carcinoma of stomach. Three died later from causes unrelated to their tuberculosis, which appeared under control. One died at subsequent pneumonectomy; 6 were late deaths from tuberculosis or its sequelæ.

In 5 patients (1·1 per cent.), as already mentioned, the disease on the thoracoplasty side seems stable but the other side is uncontrolled. In 3 of these lobectomy or pneumonectomy had been required on the thoracoplasty side. Fourteen others (3·1 per cent.) are unsatisfactory. In 11 surviving patients the thoracoplasty failed to control the underlying disease and in 1 of these subsequent resection failed also. Three patients are unsatisfactory for other reasons—recurrent tuberculous abscesses of the chest wall; severe chest pain and poor general condition; persistent amyloid disease.

The patient with severe chest pain was one of the two in this series upon whom bilateral thoracoplasty was performed; the other died three days after operation on the second side.

Salvage Cases

In 1957 Gough *et al.* published a detailed follow-up, covering six to eight years, of thoracoplasty cases operated on during 1947-49. They found that 82 per cent. were quiescent. These results were very satisfactory, especially as their patients had received little or no chemotherapy before operation. The results in our series, for patients who had been less than a year on drugs, are roughly comparable (Groups C and D, Table), and demonstrate once again that thoracoplasty is an effective, relatively safe procedure.

Between 1949 and the present day, however, and particularly during the period in which the operations of our series were carried out, the standards according to which patients were chosen for thoracoplasty changed for two main

reasons. In the first place, excision proved efficient and no longer requires special indications. Secondly, the need for surgery in some cases where, seven years ago, thoracoplasty would have been advised is now obviated by the use of long-term chemotherapy.

If thoracoplasty has, as some feel, become an operation undertaken largely where excision is impracticable, we cannot hope that future series, chosen by exclusion, will show such favourable overall results as those of the 1951-56 cases. Resection may be contraindicated by the extent of disease, to which, as Gough *et al.* have shown, the progress after thoracoplasty is closely related.

We cannot presume that future figures will compare with those of the pre-chemotherapy era—those reported by Gough *et al.*, for example, or by McHale (1949), who found sputum conversion in 80 per cent. of cases. It is true that where chemotherapy brings the disease under sufficient control, converting the sputum, and allowing a selective choice of patients, the results are excellent. Group B (Table) had received a year's or more drugs and their sputum, pre-operatively, was negative. At least 89·1 per cent. are satisfactory, without any further ipse-lateral surgery. It is unlikely, however, that the use of thoracoplasty will increase among such cases. Since resection may be contra-indicated by drug resistance, and reliance on drugs alone is hazardous where the sputum does not convert, those instances where chemotherapy failed are more significant for the future of major surgical collapse; if the drugs have not succeeded—because, for example, of fibrosis—then collapse too may fail, and the results may well be worse than among those where they have not been tried.

There were 31 patients in our series whose sputum long-term chemotherapy had failed to convert. They had received a year's or more anti-tuberculous drugs during the two years before thoracoplasty; were still positive pre-operatively. Eight (25·8 per cent.) have died. Nine of the other 415 patients are dead because of operation or of tuberculosis or its sequelæ—7 of this group of 31. 51·6 per cent. are satisfactory without ipse-lateral excision, compared with 80·9 per cent. in the series as a whole. One has been lost sight of; in another the operation side is controlled but contralateral disease active. Of 6 patients in the group who had excision performed later on the thoracoplasty side, 2 are dead (of tuberculosis; amyloid disease), 1 unsatisfactory and 3 well.

The Older Patients

35·9 per cent. of the 749 patients admitted to St. Mary's in 1957 with tuberculosis were aged 45 or over; 72·2 per cent. of those who died there of the disease. The relatively increasing numbers of older tuberculous patients present a serious problem for their response to medical treatment is often disappointing (Caplin *et al.*, 1956; Sullivan, 1958) and the quantitative importance they have assumed in chest hospital beds and the failures of chemotherapy among them threaten any arbitrary age limit for surgery: a number of reports have been published on the results of thoracoplasty and excision in such cases (Beaconsfield *et al.*, 1954; Kallqvist, 1956; Pines and Rowlandson, 1956).

Thirty-three patients of the present series were aged 45 or over. Four

(12·1 per cent.) died within three months of operation—1 of those deaths being from carcinoma of the stomach; 1 has been lost sight of, was well when last seen. The remainder are alive. Three are unsatisfactory. Twenty-five (75·8 per cent.) are satisfactory—including 1 patient who required resection. Fifteen (45·5 per cent.) have been free from any complications.

Apart from the operative mortality these figures are encouraging, but the small numbers indicate that the patients were well selected. Only 3 were in the group still sputum positive who had received a year's or more chemotherapy and none of these is satisfactory. Were thoracoplasty to be used more often as a salvage procedure in older people who have not responded adequately to drugs it is probable that the results would be depressing. There has been, naturally enough, a greater temptation to attempt salvage in the young: a persistently positive sputum in a man of 60 has seemed less terrible—once he is taught how to spread as little infection as possible—than in someone of 20. However, phthisiology, increasingly geriatric, cannot comfortably become a minor branch of chest medicine while these older problem patients are still so numerous. If thoracoplasty is to be widely undertaken among them it must be with the realisation that the mortality rate is unlikely to be low, especially in dyspnœic patients (Pines and Rowlandson, 1956), and that complete salvage of the sputum positive by such collapse therapy where drugs have failed is not much better than a fifty-fifty chance. On the other hand, the usual alternative to salvage surgery for these people will be to remain infectious and progress to full resistance: without operation, with our present chemotherapy, their expectation of life cannot be good.

Holst Thoracoplasty

According to Shaw (1958) the indications for thoracoplasty are: (1) as a consolidating procedure in limited residual disease and (2) as a salvage operation in cases unsuitable for resection.

Holst roof-plasty (Holst *et al.*, 1955), which is usually used as a consolidating measure, has æsthetic advantages over the conventional operation. Thirty-nine patients of the present series were subjected to it and have been followed for 1 to 3½ years. One who had already a conventional thoracoplasty on the other side died three days post-operatively of cardiac failure. One died later of causes unrelated to the tuberculosis, which appeared under control. Three (7·7 per cent.) have been lost sight of, were well when last seen. Thirty-one (82 per cent.) are satisfactory and had no complications, apart from asthma in one patient. In 1 the disease has been controlled since subsequent resection. In 1 the disease remains active.

These figures are good and the modified thoracoplasty seems sure of some employment in the future. But it is as a salvage procedure that thoracoplasty will be of most value and there is no use hoping for striking safety and brilliant success in desperate cases; the danger is that a useful procedure may get a bad name rather because of the material than the method.

Summary

(*a*) 85·9 per cent. of 446 patients who had thoracoplasty are satisfactory 1 to 7 years later. Another 4·3 per cent., now lost sight of, were well when last seen.

(*b*) Such good results are unlikely in the future, if thoracoplasty is to be used mainly in cases unsuitable for resection.

(*c*) The average age of tuberculous patients is increasing. Chemotherapy is prone to fail in older people and, where long-term chemotherapy has not converted the sputum, thoracoplasty is only moderately successful: it is wrong to expect brilliant results among salvage cases.

These operations were carried out by Mr. M. Hickey, Mr. B. O'Neill, Mr. D. Kneafsey, Mr. H. Wingfield, Mr. K. Shaw.

We wish to thank Dr. C. K. MacArdle, Medical Superintendent, for permission to publish this paper. We also wish to thank the many physicians in Ireland and Great Britain who by their co-operation made the survey possible.

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A FATAL CASE OF VIOMYCIN HYPERSENSITIVITY

By R. G. Benians and C. J. Pinto

From St. Luke's Hospital, Bradford

Viomycin is well known to be responsible for toxic reactions. It was given daily when first introduced for the treatment of tuberculosis and always caused albuminuria, usually within two weeks (Werner *et al.*, 1951; Schaffield *et al.*, 1954; Adcock *et al.*, 1954). Red blood cells and casts were frequently found in the urine. Other symptoms of toxicity were rarer, but maculo-papular erythematous rashes were recorded and were sometimes of such severity as to cause the treatment to be stopped.

These toxic reactions led to modification of the method of treatment, leading to the present scheme whereby an average-sized adult receives 2 g. of viomycin twice weekly in divided doses. Even this regimen is not free from risk, as Tucker (1954) found, for out of a series of 125 patients so treated, toxic effects of some sort were present in 42 per cent., and in 18 cases treatment had to be abandoned. Three of these had progressive impairment of renal function, one had severe albuminuria, two had drug fever and three had drug rashes. Renal damage on twice weekly viomycin has also been reported by Phillips and Larkin (1955).

The case which we now wish to record showed renal damage with albuminuria, drug fever and a very extensive rash. It led to a fatal conclusion.

Case History

A.W., female aged 34, developed right-sided pulmonary tuberculosis in February 1954 and despite Sanatorium and Out-Patient chemotherapy, was left with a chronic right upper zone cavity. She refused surgery, and her tubercle bacilli ultimately became streptomycin resistant, though they remained isoniazid sensitive. She could not tolerate PAS because of severe diarrhœa.

Spread to both lungs developed, despite continued streptomycin with isoniazid, after the birth of her fifth child and she was admitted to hospital in August 1957 in an acutely ill state.

She was put on to viomycin 2 g. twice weekly with oxytetracycline 4 g. daily and within four weeks her fever had settled and she was greatly improved. Twice weekly tests of the urine showed no albumen, and an X-ray taken after six weeks' treatment showed radiological improvement.

A few days later her temperature started to swing a little with evening peaks to 100° F. and a trace of albumen appeared in her urine. Despite this, she remained in good general health and it was not felt necessary to abandon her treatment. After a further two weeks of these mild toxic reactions, she suddenly became acutely ill with a fever of 105° F. and a raised blotchy erythematous

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rash involving the whole of the trunk, the face and the inside of the mouth. Her urine now showed a heavy deposit of albumen for the first time.

Her treatment was stopped and she was given a high fluid intake and antihistamines by mouth. In the absence of effective anti-tuberculous drugs, corticosteroids were not considered advisable lest they should cause further spread of her pulmonary disease. Her rash and fever were unaffected and she remained gravely prostrated. She had no oliguria and only occasional vomiting, but her blood urea stood at 175 mg./100 ml. when taken eight days after her acute illness started. After showing little change for two weeks, she started to deteriorate further and died three weeks after the first appearance of the rash.

Post-mortem Findings

The body was that of a thin female. The skin showed a slight icteric tinge and a dry, scaly eruption in patches was present. Cyanosis and œdema of the limbs were absent.

On opening the thoracic cavity extensive pleural adhesions were present on both sides. The lungs showed evidence of a fibrocaseating tuberculosis with numerous cavities involving the whole of the right lung and the apex of the left. The heart was of normal size and showed no abnormality. The peritoneal cavity and the gastro-intestinal tract showed no abnormality. The liver was slightly enlarged (weight 2,200 g.) and appeared pale. The spleen was slightly enlarged (weight 250 g.) and appeared congested. The gall bladder, bile ducts and pancreas showed no abnormality. Both kidneys were slightly enlarged (weight 280 g. each) and appeared congested with greyish-white areas in the cortex and medulla. The capsule stripped off easily.

The urogenital organs and the endocrine glands showed no abnormality. The brain showed œdema and generalised softening.

Histology. Sections of the liver, spleen and kidneys were stained with hæmatoxylin and eosin. The spleen, apart from congestion, showed no abnormality. The liver showed fatty degeneration and areas of centrilobular necrosis (Fig. 1). The kidneys showed necrosis and desquamation of the epithelium of the tubules. Hyaline and cellular casts were seen also in the tubules. The interstitial tissue appeared œdematous and infiltrated by lymphocytes (Figs. 2 and 3). The glomeruli appeared normal. Staining with Congo red showed no evidence of amyloidosis.

Discussion

It is probable that the pulmonary tuberculosis became worse in this patient during the last three weeks of her life, when she was in an acutely toxic state, and this must have contributed in part to her death. The persistence of the rash for three weeks and the high blood urea suggest that she was never able adequately to clear the viomycin from her blood stream, so that its toxic effect was prolonged indefinitely. Thus there was no histological evidence of regeneration in the renal tubules. It is possible that an artificial kidney, if available, might have been able to break the vicious circle, though the problem of treating the progressive tuberculosis would still have remained.

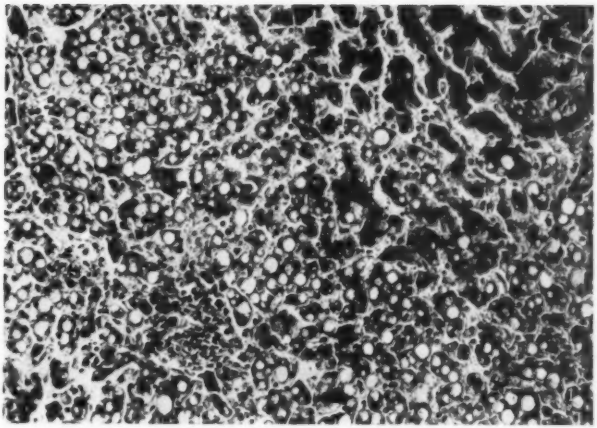

FIG. 1.—Histological section of liver showing the hepatic cells containing globules of fat (×60).

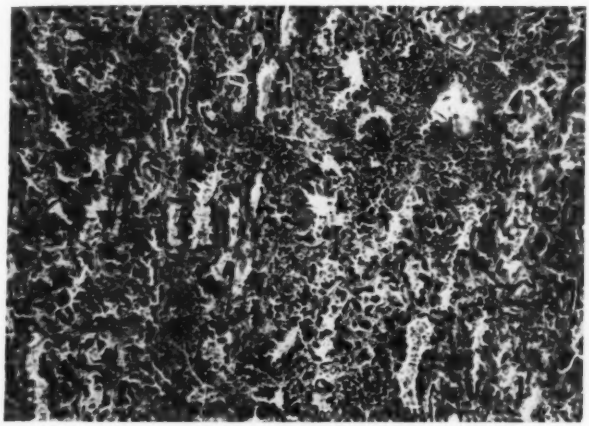

FIG. 2.—Histological section of kidney showing necrosis of the convoluted tubules and lymphocytic infiltration (×50).

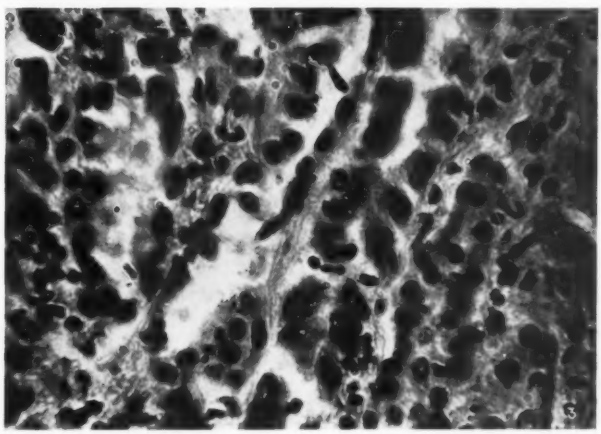

FIG. 3.—Histological section of kidney showing desquamation of the tubular epithelium (×120).

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Summary

A case is recorded of renal damage, fever and drug rash following twice weekly viomycin treatment. At post-mortem the renal tubules showed necrosis.

We wish to thank Dr. D. K. Stevenson, under whose care the patient was admitted, for permission to publish this case.

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LARYNGEAL PALSY FOLLOWING SPONTANEOUS PNEUMOTHORAX

By H. Duff Palmer and S. K. Gupta

From Harts Hospital, Woodford Green, Essex

The occurrence of laryngeal paralysis following spontaneous pneumothorax is very uncommon (Alestra, 1947; Lublinski and Ohm, quoted by di Benedetto, 1953). Such a phenomenon has, however, been occasionally observed after an artificial pneumothorax (Gualdi and Lanza, 1939; Angirany and Mounier-Kuhn, 1939; Champeux and Adrian, 1947; Piaget and Seguin, 1949; di Benedetto, 1953; Ekroth, 1956).

The following case merits description as we have been unable to trace a similar report either in the British or American literature.

Case Report

A man, aged 42, was admitted on December 10, 1957, with severe dyspnœa. He had been suffering from pulmonary tuberculosis since 1948 although his disease was regarded as "quiescent." He had also a history of chronic bronchitis for some years.

On the morning of admission he had a sudden attack of severe pain in the right side of his chest. Simultaneously he became very dyspnœic, pale and had profuse sweating. He was transferred to the hospital about ten hours later.

Clinically, on admission he appeared very pale, orthopnœic and emaciated. No history was available from the patient as his voice was reduced to an inaudible whisper. His pulse and respiration were 120 and 40 per minute respectively. His blood pressure was 115/65 mm. Hg. In spite of the absence of clinical mediastinal shift, he had all the classical signs of a spontaneous pneumothorax on the right side of his chest.

Investigation. His hæmoglobin was 89 per cent. (Sahli) and blood sedimentation was 28 mm./1 hour (Westergren). White cell count was 12,000/c. mm. with 83 per cent. polymorphs. Otherwise normal differential count. Repeated sputa failed to show any acid-fast bacilli. The skiagram of the chest confirmed the presence of a pneumothorax on the right side and the right lung was adherent at its apex and on the mediastinal surface with the surrounding structures. There was gross destruction of the lung parenchyma on both sides. No mediastinal shift was observed in comparison with previous films.

Progress. Sedation, analgesics and oxygen failed to relieve his distress. Repeated aspirations of air were done without any benefit. The intrapleural pressure remained very high (about +16 to +18 mm. of water). Hence a self-retaining Foster-Carter needle was introduced later with underwater-seal

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drainage. The lung re-expanded completely and uneventfully in about thirty-six hours.

He was kept in bed and the usual anti-tuberculous drugs were administered as a precautionary measure. His general condition improved very soon but his voice did not show any change. A laryngological examination (on January 2, 1958, by Dr. R. D. Henderson) revealed a paralysis of the left recurrent laryngeal nerve. There was no evidence of any tuberculous or malignant involvement of the cord. The patient was discharged home shortly afterwards.

Discussion

Perhaps the most important fact in the clinical story was the simultaneous onset of pain and loss of voice. The dramatic, sudden and concurrent precipitation of the spontaneous pneumothorax and the left recurrent laryngeal nerve paralysis suggests a possible interrelationship. The nerve might have been damaged mechanically owing to minimal and subclinical mediastinal shift. Ischæmic injury of the nerve might be an additional factor. The presence of an independent pathology such as bronchial neoplasm was considered but dismissed.

We are indebted to Dr. R. D. Henderson, our laryngologist, for his help.

Summary

A case of laryngeal palsy following spontaneous pneumothorax is described. The possible mode of occurrence and the relevant literature is discussed.

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THE CONSERVATIVE TREATMENT OF PRIMARY TUBERCULOSIS IN CHILDREN

A FIVE-YEAR FOLLOW-UP

By C. S. Breathnach

From the Primary Tuberculosis Clinic, Clarendon Row, Dublin

The application of modern chemotherapeutic (Cathala *et al.*, 1949; Wallgren, 1950; Debré, 1951) and thoraco-surgical measures (Thomas, 1952) to the treatment of primary tuberculosis in childhood has coincided with Holmdahl's (1950) challenge to the traditional conception of the condition as a benign one. Complications unavoidably assume a predominant rôle in surveys based on cases admitted or referred to residential institutions, *e.g.* in those of Lincoln (1950, 1951), Bentley *et al.* (1954), Walker (1955) and Cameron *et al.* (1957), and a truer picture of the behaviour of the primary complex can be gained from experience garnered in the field service, such as that recorded by Thompson (1947), Macpherson and Lutwyche (1950), Cammock and Miller (1953), Thomas *et al.* (1954), and Shaw and Wynn Williams (1956).

A five-year review is here presented of children with a primary infection among whom only a minority received " modern " treatment and then almost exclusively for complications which demanded such measures.

Material

During 1951, 465 children under 15 years of age suffering from primary tuberculosis came to the Primary Tuberculosis Clinic, Dublin, for the first time. Of this number 281 (120 boys, 161 girls) were reviewed (history, physical examination, chest X-ray) in the early months of 1957, thus ensuring that all had been at least five years under surveillance. All but 43, who had calcified primary tuberculosis when they first attended during 1951, suffered from active primary tuberculosis at the time of diagnosis, *i.e.* no case suffering from post-primary tuberculosis (no glandular enlargement discernible) at the time of discovery was included. The unavoidable sampling which occurred in the review is, as indicated in the appended Table II, not unduly biased.

Diagnosis. All cases were tuberculin sensitive: Moro positive in 177; Mantoux positive in 96 cases; and conversion in 18 cases in 4 of which it was not possible to locate the portal of entry.

The lungs were the seat of infection in 259 cases:

	Right	*Left*	*Total*
Primary complex	90	57	147
Primary focus alone	12	11	23
Glandular enlargement only ..	47	27	74
Bilateral glandular enlargement ..	—	—	15

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An extra-pulmonary primary lymphadenitis was found in 10 cases: cervical 8; inguinal 1; abdominal (tabes mesenterica), 1. In 12 cases the site of infection was not found.

In 149 cases the child was frequently in the company of an individual, usually within the family (and most commonly the father even in the youngest children; Breathnach, 1958), excreting tubercle bacilli. Infrequent contact with a known case of tuberculosis was discovered in 7 cases and the source of infection was not found in 125.

Erythema nodosum appeared in 19 girls (11·8 per cent.) and 6 boys (5 per cent.); it was not seen in any child under 2 years and occurred more frequently with increasing age:

Age group (years)	*Total number*	*Number with erythema nodosum*	*Percentage*
2-5	139	9	6·4
6-11	91	13	14·3
12-14	13	3	23·0

Phlyctenular conjunctivitis presented in 5 children and developed subsequently in another 2; 4 boys and 3 girls were affected. All cases in which these allergic phenomena were noted are now healed and well.

Treatment. In the vast majority of cases treatment was conservative:

Treatment	*Condition of primary infection*	
	Active	*Inactive*
Rest at home (4-12 months)	126	0
Sanatorium régime (6 months or longer) ..	101	4
Chemotherapy (institutional)	11	2
Nil	0	37

Streptomycin and para-aminosalicylic acid were given to 10 children and were combined with isonicotinyl hydrazide for 3. Right upper lobectomy was performed in 1 child and excision of glands was carried out in 4 cases presenting with peripheral lymphadenitis.

Results

Pulmonary Complications. Pulmonary complications arose in 102 cases, all originally pulmonary primaries. In 52 cases extensive glandular enlargement (*i.e.* when the hilar shadow exceeded 1 cm. in diameter, in children under 2 years when the glandular shadow extended beyond the cardiac outline, or, when the superior mediastinal glands were secondarily involved). In 46 cases, including 11 with extensive glandular enlargement, segmental lesions (epituberculosis, atelectasis, consolidation-collapse) were seen. Pleural effusion complicated 15 cases, in 1 case preceding a segmental lesion and later in another which had shown extensive glandular enlargement. In no instance did local or general (pneumonic) miliary tuberculosis develop nor was cavitation of the primary focus encountered in any child. Tertiary tuberculosis (single-organ, chronic or adult phthisis) appeared in 2 children. Calcification was

TABLE I.—PULMONARY COMPLICATIONS IN RELATION TO INFLUENCING FACTORS AND OUTCOME

	Age	Total	Percentage	Male	Female	0-14	14+	Tuberculin	Good	Frequent contact	Erythema nodosum	Rest	Sanatorium	Chemotherapy	Healed	Pulmonary sequelæ	Tertiary disease	Extra-pulmonary complications	Death
		259		113	146	42	94	108	151	138	22	109	100	13					
1A. Extensive glandular enlargement	0- 1	17	47·2	8	9	0	7	10	7	14	0	5	10	2	15	1	0	1	1
	2- 5	26	20·6	8	18	7	7	16	10	11	2	7	18	1	23	2	0	1	1
	6-11	7	8·2	3	4	3	2	4	3	4	1	5	1	1	7	0	0	0	0
	12-14	2	16·7	0	2	0	2	0	2	1	0	2	0	0	1	0	1	0	0
	Total	52		19	33	10	18	30	22	30	3	19	29	4	46	3	1	2	2
	Per cent.	20·1		16·8	22·6	23·8	19·2	27·8	14·5	21·7	13·6	17·4	29·0	30·8					
1B. Segmental lesions	0- 1	8	22·2	4	4	0	2	6	2	7	0	0	7	1	5	2	0	1	1
	2- 5	26	20·6	11	15	5	11	14	12	14	1	4	21	1	21	4	0	1	1
	6-11	12	14·1	8	4	2	4	5	7	2	3	8	2	2	10	2	0	0	0
	12-14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Total	46		23	23	7	17	25	21	23	4	12	30	4	36	8	0	2	2
	Per cent.	17·8		20·4	15·7	16·7	18·1	23·1	13·9	16·7	18·2	11·0	30·0	30·8					
1C. Pleural effusion	0- 1	3	8·3	1	2	2	0	1	2	2	0	0	3	0	3	Number of Pulmonary Primary Infections in each Age Group			
	2- 5	5	4	3	2	0	2	3	2	1	0	2	2	1	5				
	6-11	7	8·3	4	3	2	3	1	6	2	1	3	4	0	7				
	12-14	0	0	0	0	0	0	0	0	0	0	0	0	0	0				
	Total	15		8	7	4	5	5	10	5	1	5	9	1	15	Total:			
	Per cent.	5·8		7·1	4·8	9·5	5·3	4·6	6·6	3·6	4·5	4·6	9·0	7·7					

Number of Pulmonary Primary Infections in each Age Group															3	36			
															5	126			
															7	85			
															0	12			
															Total:				259

present in 43 cases on initial examination and was detected in another 142 subsequently—almost exclusively before the end of the second year of observation.

Extensive glandular enlargement occurred with significantly greater frequency in younger children (Table 1A); of 52 children, 43 or 82·7 per cent. were under 6 years of age. It was more common, significantly at the 5 per cent. level, when housing conditions were poor. Only 6 children failed to make a complete recovery and in these the glandular involvement could not be said to have contributed directly to this failure.

Segmental lesions appeared rather more often in cases with extensive glandular involvement, in 21·2 per cent. as against 14·4 per cent. in those without. Almost three-quarters of all segmental lesions were seen in children under 6 years and all occurred in children under 12. From Table 1B an attempt has been made to examine the relationship of segmental lesions to various factors, but on fragmentation the numbers are too small to justify any firm conclusions. Non-tuberculous sequelæ, however, play a major rôle in post-infective morbidity and of the 44 survivors in which segmental lesions had been present 8 show some incapacity:

Recovery with apparently full re-expansion	26
Linear contraction with partial re-aeration (symptom-free) ..	10
Clinical or radiological evidence of bronchial damage ..	8

The sequelæ in the 8 children are:

Persistent segmental shadow but no symptoms	3
Middle lobe syndrome (symptoms severe in 1)	3
Bronchiectasis	2

Notable sequelæ remain in 2 of the 12 segmental lesions treated at home and in 6 of the 30 treated in a sanatorium. No evidence of bronchial damage is present in either of the 2 surviving cases which received chemotherapy.

Pleural effusion did not develop in any case after the third month of observation. The distribution in relation to possible causative factors is indicated in Table 1C, but the numbers are too small to determine whether the incidences in the various groups differ significantly. All 15 children are now clinically and radiologically well (but it should be noted that no effusion was seen in the small group of children over 11 years of age).

Progression to tertiary tuberculosis was discovered in 2 children (a boy and a girl) in the fourth and fifth years of observation respectively; in both the primary complex was calcified at the time of diagnosis. If the children are too young to have reached the age when tertiary lesions are likely to occur (the two youngest age groups) the incidence of tertiary disease is almost 2 per cent. In both cases a satisfactory response to chemotherapy was obtained.

Extrapulmonary Complications. Complications outside the lungs developed in 6 of the 259 pulmonary primary infections:

	Total	*Fatal*	*Recovered*
Tuberculous meningitis	3	3	0
Skeletal tuberculosis	3	1	2

Remote glandular involvement followed peripheral lymphadenitis in 2 cases.

Mortality. Three deaths occurred due to meningitis and 1 to widespread skeletal tuberculosis; paratracheal glandular enlargement was present initially in 3 of the 4 cases. Two of the 38 children in the 0-1 year group and 2 of the 139 children in the 2-5 year group died, giving an overall death rate of 1·4 per cent. or a rate of 2·3 per cent. in children under 6 years.

Discussion

Prognosis was little influenced by environmental factors or allergic phenomena. In view of the ætiological rôle of glandular enlargement in segmental lesions (Wood, 1939; Laff *et al.*, 1951), the similar age incidence and frequent association of extensive glandular involvement and segmental lesions was noteworthy. The former, however, especially superior mediastinal involvement, commonly preceded fatal hæmatogenous dissemination, while permanent non-tuberculous bronchopulmonary damage was a likely sequel of the latter. The fact that pleural effusions were confined to children under 12 years (the oldest age group was very small numerically) may help to explain the good prognosis so far encountered in these cases, for there is general agreement with Nathhorst (1948) and Bentley *et al.* (1954) that tertiary disease, which in any event is seldom seen in children under 10 years (Zacks, 1939), is far more likely to follow effusion in older than in younger children. Tertiary lesions developed in 2 of the older children entering the survey with calcified primaries—an apparent confirmation of Myers' (1938) contention that calcified primary infection carries a darker prognosis.

Rest (3 to 6 months) was recommended in all cases of active primary infection and where pulmonary complications were present admission to sanatorium was advised. The results, therefore, are of little value in assessing the need for institutional treatment. Bentley *et al.* have demonstrated that *prolonged* sanatorium treatment is unlikely to be valuable or necessary, but Cameron *et al.* (1957) commend the " ordered and tranquil life of a children's sanatorium."

A condition in which the mortality rate is 5 per cent. in children under 2 years and 2 per cent. in children under 6 years can hardly be termed benign, and it is not surprising that the newer chemotherapeutic agents should be utilised to prevent the fatal complications likely to arise in younger children. In attempting such chemoprophylaxis three facts must be considered: firstly, the protection given is incomplete (Lorber, 1950; Walker, 1955; Bentley *et al.*, 1954; United States Public Health Service, 1957); secondly, the incidence of segmental lesions may be higher in drug-treated mediastinal lymphadenitis (Bentley, 1955); and thirdly and most important, miliary tuberculosis and meningitis are most frequently seen in the wake of sub-clinical primary infection (Price, 1948; Bentley *et al.*, 1954) so that prevention of the primary infection rather than its complication is the aim. Certainly with children born into a tuberculous environment (in large cities in these islands, tuberculosis in the family) B.C.G. vaccination is a more rational preventive measure than chemoprophylaxis. The only effective alternative is yearly (or half-yearly)

TABLE II.—THE REVIEWED GROUP AS A SAMPLE OF THE TOTAL NUMBER REGISTERED

	Age (years)				*Sex*		*Family income per head*		*Housing*		*Contact*			*Allergy*		*"Disease"*				*Treatment*				*Total*
	0-1	2-5	6-11	12-14	*Male*	*Female*	0-14	14+	*Tenement*	*Good*	*Frequent*	*Infrequent*	*Nil*	*Erythema nodosum*	*Phlyctenular disease*	*Simple pulmonary P.C.*	*"Complicated" pulmonary*	*Non-pulmonary*	*Unsited*	*Rest*	*Sanatorium*	*Chemotherapy*	*Nil*	
Registered 1951 ..	55	209	182	39	209	256	103	166	197	268	253	9	203	35	20	266	162	12	25	236	157	20	52	465
Outcome known (reviewed 1957 plus deaths)	38	139	91	13	120	161	46	101	116	165	149	7	125	25	7	157	102	10	12	126	105	13	37	281
Expected response ..	33·2	126·2	97·8	23·6	126·2	154·6	62·2	100·3	118·9	161·9	152·8	5·4	122·6	21·1	12·1	160·7	97·8	7·2	15·1	142·5	94·8	12·1	31·4	
	$p<.001$				$.3>p>.2$		$p<.001$		$.7>p>.5$		$.8>p>.7$			$.9>p>.8$		$.9>p>.8$				$.01>p>.001$				

serial tuberculin testing, an arduous and expensive task if extensive; as Bentley *et al.* stress, " before treatment for primary pulmonary tuberculosis can be initiated the condition has to be diagnosed."

Resection is the only answer to permanent bronchopulmonary destruction following a segmental lesion. In addition, acute respiratory distress in recent primary infection may, as Thomas has shown, require hilar adenectomy with or without ablative surgery. For glandular enlargement without acute distress, however, hasty surgical intervention as advocated by Chesterman (1957) and Hughes and Ray (1958) is not indicated, for Seal and Thomas (1956) found reversible changes in some of the segments removed in the early phase of infection and eventual re-expansion or re-aeration occurs in a majority (82 per cent.) of cases.

Conclusions and Summary

281 children representing a fair if not unbiased sample of the 465 children under 15 years discovered to have primary tuberculosis in 1951 have been reviewed 5 years later. Treatment was almost exclusively conservative.

In the young child primary tuberculosis carries two grave dangers: (i) hæmatogenous dissemination, often associated with extensive glandular enlargement; and (ii) permanent bronchopulmonary damage in the wake of a segmental lesion.

In the older child the condition is more benign, with progression to tertiary disease the most common complication, the risk being greatest in cases complicated by pleural effusion (unconfirmed) or in which calcification has appeared.

Chemoprophylaxis of dissemination is indicated in children under 2 years with established primary infection, but B.C.G. vaccination of children born into a tuberculous environment is recommended as the more rational preventive measure. Surgical intervention, unless acute respiratory distress supervenes, is only necessary when irreversible bronchopulmonary damage is present.

I am very grateful to Dr. J. B. O'Regan, City Medical Officer, for this assignment, the execution of which whould not have been possible without the work and help of Drs. M. Dunlevy and K. O'Flaherty. My thanks are also due to Miss A. Boland, S.R.N., R. Black, M.S.R., and E. MacCarron, M.S.R., for the assistance gladly given and to Dr. D. McCarthy and Mr. J. Knaggs, Central Statistics Office, for their advice.

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THE THIRD INTERNATIONAL CONGRESS OF PHOTOFLUOROGRAPHY

Stockholm, August 20-23, 1958

By Owen Clarke

From the Chest Clinic, Canterbury

This Congress was organised by the International Society of Photofluorography and the International Union against Tuberculosis.

In his Presidential Address, Professor Carl Wegelius welcomed the delegates from thirty-five countries who represented many important national organisations and various branches of medicine.

He hoped that the term Radiophotography—RP—would become standardised for this branch of roentgenology which was developing rapidly along its own lines. Radiophotography, of course, had its origin in tuberculosis work and this was still its most important role both for surveys and clinical work in connection with chest diseases, but it was becoming increasingly important in cardiology, gastro-enterology, and study of diseases of the skeleton.

These aspects were enlarged upon by the speakers in the Congress, although the greatest emphasis lay upon chest diseases and many papers were devoted to descriptive and statistical accounts of survey work in different parts of the world.

Discussion of Papers

Professor M. de Abreu (Brazil) and Professor G. Babolini (Italy) opened the Congress with stimulating accounts of their work and of the wider possibility of RP in non-pulmonary disease; Professor Etienne Bernard (France) described its diagnostic value in pulmonary tuberculosis, and Dr. Owen Clarke (Great Britain) summarised the advantages of this technique for outpatient work in chest clinics and emphasised the criteria which must be fulfilled if RP were to supplement full-size films.

In the session dealing with radiation hazards, Dr. A. Nelson (Sweden) discussed the recent U.N. report and other speakers confirmed the relatively small dosage due to radiophotography. The figures of Dr. L-E. Larsson (Sweden) were of particular interest. Dr. B. Hauson (Germany) and Dr. C. Buckheim (Germany) both described new techniques using high K.V. and special contrast developers by which the skin dosage was greatly reduced.

A discussion on the use of Radiophotography for tuberculosis and other chest diseases concentrated too much on survey work, but the reports of Dr. F. T. Jarman (Great Britain) and Professor R. Griesbach (Germany) covered long periods of survey. Dr. Jarman described fourteen years' survey work in Wales and pointed the lessons to be learned from the results.

Dr. K. Liebschner (Germany) reminded members that the cost of detection was much less than of treatment, and an interesting paper by Dr. Ch. Couhy (France) outlined the valuable work done in Professor Bariéty's clinic in Paris.

Lung cancer was first considered by Dr. F. A. Nash (Great Britain), who did not consider that an annual X-ray was frequent enough to be of great value in this disease.

Among the many papers dealing with diagnosis, Dr. Philip Ellman (Great Britain) dared the sharp reminder that diagnosis is the duty of a clinician and cannot rest on radiology alone. He showed many chest films associated with various connective tissue pleural and pulmonary lesions which could easily be described as due to pulmonary tuberculosis unless the whole clinical picture were known.

Naturally such a Conference also discussed the human factor in X-ray reading, so dependent upon good technique. The excellent display by many firms gave a background to these papers, and also to the use of radiophotography in cardiac disease, bone diseases and gastric investigation. These ideas, relatively untried in this country, are already widely used abroad.

Hospital Visits

In addition, the Congress included visits to the Karolinska Thoracic Unit and many other clinics and sanatoria as well as a most hospitable and interesting social programme. These visits showed a standard of hospital design and equipment which is still almost unknown here, and indeed there is little evidence that our plans even aim at such a high target. Much of it would be considered extravagant and admittedly is not essential for good medicine, but it indicates an adventurous and progressive state of mind.

Attendance at Conferences

There were more than 500 delegates at the Conference: only six doctors were from Great Britain. Of these, four had been invited to contribute papers and one of us had the privilege of being chairman for a session.

There were more than sixty delegates from both Germany and Italy.

Many of our Swedish hosts much regretted that Great Britain was so lightly represented at such international congresses, especially since the opinions and work of our doctors is so highly respected. Representatives of other countries, too, expressed the wish to hear more of British medicine.

Of course, the question of cost arises: so too in other countries. Much credit is due to those authorities who recognise a responsibility to help ensure that British representation abroad is maintained: their example should be more widely followed.

But, in addition, a responsibility rests on British doctors themselves to accept the cost and to attend international conferences, even if not invited to read a paper. If we are proud of a Health Service and of our own work other countries should hear of our pride and meet our representatives.

How many of our doctors or administrators have in fact seen and known the standards established in Sweden, Canada, France or Germany? How many of our doctors are prepared to deliver a paper in a foreign tongue or publish in a foreign journal? How many know the excitement and stimulus of discussion with experts of other countries, and the value of these friendships?

The Stockholm Conference showed an international approach and a variety of ideas from which we could benefit: we too have much to offer to international thought. Doctors of all nations should think with a world mind: but that involves contribution and absorption of world views which can only be done by the personal contacts which stimulate understanding, adventure and vision.

REVIEWS OF BOOKS

Tuberculosis: Every Physician's Problem. By J. ARTHUR MYERS, M.D. Springfield, Illinois: Charles C. Thomas (Blackwell, Oxford). Pp. 290. Illus. 57s. 6d.

This small book purports to give physicians who are not specialising in chest diseases an account of modern views on tuberculosis as it affects the human body, and its prevention. It is divided into two parts. In one there is a lucid account of the pathogenesis and occurrence of the disease as it affects the various organs, and appropriate treatment. It is necessarily brief, but the best use is made of the limited space. European workers will not all concur in Dr. Myers's view of the benign nature of the primary lesion in young adults; and the advice that an uncomplicated tuberculous pleural effusion should be treated by six months' bed rest and six months' rehabilitation seems drastic indeed.

The second half of the book is concerned with Dr. Myers's views on eradicating tuberculosis. Although he does not say so, his main ideas must be applicable only to a community where tuberculous infection is light, such as the U.S.A. For eradicating tuberculous *infection* in the U.S.A. he feels that tuberculin reaction is essential, and he advocates its frequent and regular use in many groups of individuals. This means that he would abandon the use of B.C.G. or any other living vaccine which would invalidate the tuberculin test. He enumerates other objections to its use, but these seem rather special pleading. The remainder of his advice on preventive measures is sound, and can only be criticised by those who believe that individual freedom of choice is preferable to compulsion. This excellent book is what we should expect from Dr. Myers. He sets out clearly the views of a very distinguished and capable physician who is at the same time a heretic.

F. H. YOUNG.

Cardiac Problems for Chest Physicians. An NAPT Symposium. Pp. 39. 5s.

Carcinoma of the Lung. An NAPT Symposium. Pp. 48. 6s.

Respiratory Disease and the General Practitioner. By C. H. C. TOUSSAINT. Pp. 28. 7s. 6d.

Modern Drug Treatment in Tuberculosis. By J. D. Ross. Pp. 46. 5s.

All published by the N.A.P.T.

The National Association for the Prevention of Tuberculosis has published four useful handbooks—two of them reports of symposia held under its auspices —which, although time and space do not enable them to probe any subject very deeply, deal with the essential problems of current interest.

The Association is to be congratulated on obtaining contributions from authorities in each subject surveyed, and we note with pleasure that it no longer confines itself to pulmonary tuberculosis in particular, or even diseases of the lung in general, but has recognised that the heart also lies in the thoracic cage.

The symposia on cardiac problems and carcinoma of the lung were respectively under the able chairmanship of Dr. Shirley Smith and Dr. Lloyd Rusby. Both subjects have considerable social, economic and medical significance at the present time and the two reports are eminently informative to those who wish to know more of either subject.

The other two booklets are designed in each case for a specific public—

respiratory disease is constantly encountered by general practitioners, who will certainly value Dr. Toussaint's work in pin-pointing the essentials in diagnosis and treatment of such diseases. The illustrations are particularly valuable.

"Modern Treatment in Tuberculosis" is intended primarily for nurses and provides a most excellent and concise introduction to the subject of anti-tuberculous chemotherapy and will be welcomed also by students and practitioners. This volume is perhaps the most penetrating in its survey, and the discussion on "salvage" chemotherapy, where the patient's organism is resistant to the standard drugs, is excellent.

In these slender volumes much ground has been covered, the material is well presented and the information can be easily assimilated.

PHILIP ELLMAN.

Major Surgery for Pulmonary Tuberculosis. By R. S. FRANCIS and M. P. CURWEN. London: MacGibbon and Kee. Pp. 95. 12s. 6d.

This monograph is a statistical survey of the results of surgical treatment of pulmonary tuberculosis for a twelvemonth period ending in April 1954. In all 8,236 patients were registered in this time. The surgery was undertaken by 75 surgeons in the United Kingdom.

6,050 cases were analysed. Those with fistulæ, bilateral active disease and empyemata were excluded. They were followed up, largely through their chest clinics, for a minimum period of two years.

The operations were divided almost equally between collapse and resection procedures, and the opportunity has been taken to discuss the relative merits of the two: there seems to be little to choose between them. The figures are analysed in detail in a series of appendices at the end of the book.

In the assessment of the results, age, sex and site of the disease are considered and the pre-operative sputum state and length of the courses of chemotherapy are all analysed. Operative mortality and the incidence of complications and their causes are also discussed.

The section discussing the figures is, I think, too short. The authors have been unduly self-disciplined and they could easily have spread themselves more. The figures they have produced are fascinating and of great importance; and although they have been allowed to speak for themselves, lazy readers would have appreciated a more extensive summary.

This comment must not be thought to detract in any way from the merit of the report; rather the opposite. For everyone interested in the surgical treatment of pulmonary tuberculosis this book is a "must," as it contains the answers to a large number of questions which have hitherto only been given on a conjectural or an intuitive basis.

J. R. BELCHER.

Tuberculosis in Animals and Man. A Study in Comparative Pathology. By JOHN FRANCIS. London: Cassell and Co. Pp. 357. Illus. 5 gns.

This admirable reference work brings together in one volume a mass of information on various aspects of veterinary and medical tuberculosis. Approximately one-third is devoted to bovine infection, dealing with its incidence, pathogenesis and pathology, its diagnosis and immunological aspects, and with its control. Bovine types of infection occurring in man and tuberculosis-like

conditions of doubtful ætiology such as the so-called "skin tuberculosis" of cattle are described. Much statistical detail is clearly set out in tables.

Most of the remainder of the work deals with tuberculosis of some thirty different animals other than bovines. All the reliable information available on each species is summarised. Finally, Professor Francis makes a detailed comparison between the types of tuberculosis occurring in various animals. Emphasis is laid on the association of characteristic tubercle formation with the existence of high degrees of allergy to tuberculin.

There are more than 100 figures to illustrate the text, of which the photomicrographs alone fail to reach the high quality of the work as a whole. The bibliography is helpful in being critically selected and, therefore, not unnecessarily extensive.

This volume satisfies a great need at this time when interest is being taken in virulence of the mycobacteria and when so much effort is being directed towards control and elimination of human and bovine diseases due to acid-fast bacilli.

R. W. RIDDELL.

Chirurgie d'exérèse dans la Tuberculose Pulmonaire. By D. HONORÉ. Paris: Masson. Pp. 216, 11 figs. and 74 tables. 3,300 fr.

The author spent several months in London in 1946 studying the technique of chest surgery, and it appears to have been this experience which formed the basis of his subsequent work in Liège.

He points out that the acquisition of antibiotics and chemotherapeutic compounds has not reduced the number of indications for surgical intervention in pulmonary tuberculosis. He considers that this is because the lesions tend to recur after the cessation of antibiotic treatment, and that excision has its part to play in removing residual foci which might light up again in later life.

The book contains a full account of his operative procedure in resection and in a variety of complications. He concludes that the incidence and prognosis in early bronchial fistula, and in most other post-operative complications, depends upon the number and sensitiveness of tubercle bacilli present in the sputum. In fact, he makes the point that the prognosis is best when there are few or no bacilli in the sputum, and when those present are sensitive to antibiotics. This would appear to be a very sound conclusion, but 3,300 francs seems to be a heavy price to pay for the information.

JAMES MAXWELL.

Medizinische Röntgentechnik. Edited by Prof. Dr. H. SCHOEN. Vol. II. Physico-Technical section. By Dr. ERICH BUNDE and Dr. VIKTO LORCK. Stuttgart: Georg Thieme. Pp. 463. Illus. DM.48.

This is the second edition of a work which was first published in 1951. It now appears enlarged and almost completely rewritten in view of the rapid development in the past seven years of X-ray technique, radioisotope therapy, radiation dosimetry and, above all, of the importance of radiation protection in this age of atomic medicine.

It is, as the authors point out, no longer possible for either the X-ray diagnostician or the radiotherapist to be competent at his work without a working knowledge of the principles of radiation physics and of apparatus design. This book is intended to provide this basic knowledge in a simple, readily assimilable form, demanding only the minimum groundwork of general physics.

In this object the book succeeds well. Its scope is comprehensive, including both radiodiagnosis and radiotherapy. There is an excellent introduction on atomic physics, brief but adequate, followed by chapters on radiation physics, X-ray photography and X-ray apparatus. The sections on radiotherapy call for special mention, as also that on radiation protection, which covers the precautions necessary in diagnosis, in therapy and in the use of radioactive isotopes.

This is a valuable work, admirably printed, bound and illustrated.

W. M. LEVITT.

Atlas und kurzgefasstes Lehrbuch der Phonokardiographie und verwandter Untersuchungsmethoden. By K. HOLLDACK and D. WOLF. Second edition. Stuttgart: Georg Thieme. Pp.179, 160 illustrations. DM.49.50.

That a second edition of this book should have become necessary after two and a half years is a testimony to its popularity. It contains chapters on the physics of phonocardiography, on the practical aspects of recording phonocardiograms, arterial and venous pulse tracings, respiration and œsophageal pulsations, while the main part is devoted to the interpretation of normal and pathological records. The reproduced records show several (up to four) phonocardiograms of different frequencies obtained from the same point of the chest, together with one or two electrocardiograph leads and a mechanical record (mostly carotid or venous pulse tracing). All were taken on paper and some phonocardiograms were recorded with a direct writing instrument. In these respects the technique differs from that usually adopted in this country. Detailed legends to the figures contain much relevant information. This book is obviously based on extensive experience obtained on large number of patients and it should be valuable to those who are thoroughly familiar with this method and with the relations between acoustic phenomena and cardiodynamics. A reader not so equipped is likely, perhaps, to lose his way among the infinite details incorporated in the text as well as in some of the legends, some of which seem to be only of theoretical interest. Furthermore, not all the authors' views are likely to be accepted without reservation in this country, *e.g.* that the first heart sound is caused by vibrations due to the sudden apposition of the ventricular wall around its incompressible contents, that aortic stenosis is rare, nor some of the comments on atrial septal defect. However, to a reader willing to study critically the impressive number of observations and their detailed interpretation, this well-produced book, with a bibliography containing 270 references, can be thoroughly recommended.

A. SCHOTT.

BOOKS RECEIVED

The following books have been received and reviews of some of them will appear in subsequent issues.

Emotional Factor in Pulmonary Tuberculosis. By David Kissen. London: Tavistock Publications. Pp. 246. 35s.

The Chemistry and Chemotherapy of Tuberculosis. By Esmond R. Long. 3rd edn. London: Baillière, Tindall and Cox. Pp. 450. 96s.

Annual Report of the Medical Officer of Health, Northamptonshire County Council, for the year 1957. Pp. 76.

Brompton Hospital Reports, Vol. XXVI, 1957. London: Lloyd-Luke. Pp. 308. Illus. 15s.

Neoplastic Disease at Various Sites. Vol. I. *Carcinoma of the Lung.* Edited by J. R. Bignall. London: E. and S. Livingstone. Pp. 298. 55s.

Notes on the Diagnosis of Occupational Diseases. London: H.M. Stationery Office. Pp. 50. 3s.

Physiotherapy in Chest Diseases. By Torsten Bruce, Caroline Reutersward and Birgit Westin. London: NAPT. Pp. 98.

The Bacteriology of Tuberculosis. By E. Darzins. Minnesota University Press and Oxford University Press. 1958. Pp. 488. 80s.

Tuberculosis in White and Negro Children. Vol. I. *The Roentgenologic Aspects of the Harriet Lane Study.* By Janet B. Hardy. Pp. 122. Illus. 60s.

Vol. II. *The Epidemiologic Aspects of the Harriet Lane Study.* By Miriam E. Brailey. Pp. 103. Harvard University Press. (Oxford University Press.) 36s.

Roentgenology of the Chest. Edited by Coleman B. Rabin. Illinois: Chas. C. Thomas (Blackwell, Oxford). Pp. 484. Illus. £7 7s.

The Observer Error in Multiple Interpretation of Photofluorograms. By Hanns J. Bauer. Copenhagen: Ejnar Munksgaard. Pp. 89.

Le Pneumothorax Spontane non Tuberculeux de l'Adulte et son Traitement. By André Meyer, J. P. Nico and J. Carraud. Paris: Masson. Pp. 144. Illus. Fr. 1,950.

Le Mediastin et sa Pathologie. By N. Bariéty and C. Coury. Paris: Masson. Pp. 854. Illus. Fr. 11,000.

Tuberkulose-Bucherei. Aktuelle Probleme der Kindertuberkulose. By Prof. Dr. H. Wissler. Stuttgart: Georg Thieme. Pp. 70. Illus. DM.11.50.

Funktionelle Röntgendiagnostik des Mediastinums am Beispiel des Bronchial-Karzinoms Demonstriert. By Priv. Doz. Dr. Med. R. Kraus. Stuttgart: Georg Thieme. Pp. 55. Illus. DM. 8.40.

Klinisch-rontgenoligische Differentialdiagnostik der Lungenkrankheiten. By Lasar Dünner. Stuttgart: Ferdinand Enke. Pp. 362. Illus. DM.69.

Handbuch der Tuberkulose. By Prof. Dr. J. Hein, Prof. Dr. Dr. h.c. H. Kleinschmidt and Prof. Dr. E. Uehlinger. Stuttgart: Georg Thieme. Pp. 832. DM.178.

Roentgenanalyse der Neugeborenen- und Saeugerierlunge. By Zoltan Zseboek. Stuttgart: Georg Thieme. Pp. 160. Illus. DM.75.

" *Die Dystrophie*"—*Spätfolgen und Dauerschäden.* By Dr. E. Goetz. Stuttgart: Georg Thieme. Pp. 202. DM.19.60.

Die Entwicklung der Tuberkulosebehandlung Seit 100 *Jahren.* By G. Domagk, L. Heilmeyer, H. Krauss. Stuttgart: Georg Thieme. Pp. 47. DM.12.

Rontgenanatomie der Neugeborenen-und Sauglingslunge. By Dr. med. habil. Z. Zsebok, Budapest. Stuttgart: Georg Thieme. Pp. 160. Illus. DM.67.50.

Tuberkulose-Bucherei. Neue Tuberkulostatika und Tuberkulostatika-Resistenz von Tuberkelbakterien. By Doz. Dr. A. M. Walter. Stuttgart: Georg Thieme. Pp. 152. DM.19.80.

REPORTS

THE BRITISH TUBERCULOSIS ASSOCIATION

THE Annual Conference of the British Tuberculosis Association formed part of the Commonwealth Chest Conference and was held in the Festival Hall, London, from July 1 to 4. The subjects for discussion were as follows:

" Towards the Elimination of Tuberculosis from Great Britain," opened by Professor J. Crofton and Dr. T. Gedde Dahl of Oslo, among others.

" The Management of the Heart in Chronic Respiratory Disease." At this session, Dr. John Briggs, Minnesota University, taking as his subject " Cor Pulmonale," surveyed the whole field of physiology, causation, clinical presentation and treatment, with special emphasis on the cardiac rather than the respiratory problem. A panel discussion followed, at which Dr. J. L. Livingstone, Dr. Paul Wood, Dr. N. J. England and Dr. W. Whitaker answered questions from the audience. Although many of these concerned clinical management of cor pulmonale, considerable interest was shown in the importance of preventing the development of heart failure, the value of antibiotics for chronic chest infection and the management of social background. The chest physician can play a valuable role in this condition. The chair was taken by Dr. Robert Platt, President, the Royal College of Physicians of London.

" Thoracic Surgery in Pulmonary Tuberculosis," the opening speakers being Sir Clement Price Thomas, Mr. Andrew Logan and Dr. J. Maxwell Chamberlain of New York.

Short papers were read by:

Dr. R. W. Riddell, Consultant Clinical Bacteriologist, Brompton Hospital, London, who spoke on " Fungus Disease of the Lung " and presented a full survey illustrated by excellent photography. He naturally concentrated on the variety of pathological findings in this country and abroad, but also touched upon the clinical aspects of diagnosis and treatment.

Professor J. Gough, Professor of Pathology and Bacteriology, Welsh National School of Medicine, Cardiff, spoke on " Pneumoconiosis." He discussed the influence of tuberculosis in dust diseases of the lung, mentioning the relative rarity of tuberculosis in miners at the beginning of the century and the greater prevalence today. The effect of this on pneumoconiosis and the consequently more serious prognosis in miners was emphasised, supplying the evidence which incriminated tuberculosis in the development of P.M.F. in coal pneumoconiosis.

Dr. J. G. Scadding, Dean and Director of Studies, Institute of Diseases of the Chest, London, spoke on " Sarcoidosis " and surveyed the relationship between sarcoidosis and tuberculosis. These conditions were not incompatible and, indeed, had much in common. Dr. H. Israel, Associate Professor of Medicine, University of Pennsylvania, described his experiences of the disease and its management at his clinics in the U.S.A.

NAPT COMMONWEALTH CHEST CONFERENCE

THE Commonwealth Chest Conference which incorporated the Annual Conference of the British Tuberculosis Association was held from July 1 to 4, and comprised lectures, discussions and clinical meetings. Subsequently, visits to hospitals, clinics and rehabilitation centres were arranged.

One of the most noteworthy points about the Conference programme was the range of subjects covered. The activities of the NAPT now included diseases

of the chest and heart, and chronic bronchitis, heart disease and lung cancer were all discussed. Other subjects included pneumoconiosis, fungus disease and leprosy. The sessions dealt not only with the treatment of chest disease, but with the whole field of prevention and rehabilitation and with the care of the patient's family. Much stress was, therefore, laid on the importance of combining the efforts of administrators, medical personnel, representatives of industry, voluntary organisations and the general public in any campaign against disease, especially from the preventive aspect.

An NAPT session of unusual interest was that on " Tuberculosis and Leprosy—Resemblances and Divergences in Diagnosis and Treatment." The general opinion was that a close integration of tuberculosis and leprosy programmes was desirable.

During the discussions on " Mass Radiography—Past, Present and Future," several speakers dealt with the fear of radiation from examination, a matter now very much in the public mind. Dr. J. F. Loutit, Director, Radiobiological Research Unit, Atomic Energy Research Establishment, Harwell, said there was no risk of genetic effects, and, dealing with somatic effects, refuted the suggestion that the probability of neoplastic change rises in direct proportion to the total dose of radiation, however delivered. He said that further research on this subject was needed and that in the meantime we should, where possible, reduce by physical means the doses given in diagnostic radiology.

Dr. Daniel Jenkins, Associate Professor of Medicine, Baylor University College of Texas, U.S.A., discussed the risks of radiation exposure in mass miniature radiography in America, as applied to his own area in Houston, suggesting that the cross-sectional approach might no longer be the most efficient method of using mass radiography and that contact follow-up might now yield better results. Various speakers, including Dr. J. E. Geddes, Consultant Chest Physician, Glasgow, gave particulars of the immense achievements of mass radiography campaigns and their value, which seems far to outweigh the small and problematical risk involved.

At the discussion on " The Heart Patient in Everyday Life " varied aspects of cardiac disease were dealt with by specialists and laymen. Professor C. Bruce Perry, Bristol University, in a paper on acute rheumatism in children as a cause of heart disease, said that this complaint was related to overcrowding and poverty and resulted from streptococcal infection—a condition which could be treated by penicillin or sulphonamides.

During the session on " Respiratory Disease—a Malady of Environment," much attention was paid to chronic air pollution in large cities as a factor in chronic bronchitis and lung cancer. Mr. Arnold Marsh, Director, National Society for Clean Air, London, gave figures showing the extraordinary amounts of atmospheric pollutants found in Great Britain.

Very great interest was aroused by the closing session of the Conference, " The Problem of Lung Cancer," and by the discussions on cigarette smoking as one of the chief causes. Dr. C. H. C. Toussaint, President of the B.T.A., said that the present epidemic of bronchial carcinoma was due to inhalation of carcinogens in cigarette smoke. Prevention was the only real remedy, but speedy investigation and diagnosis could lead to prompt surgical excision and the saving of many lives. It was felt that it was vital to try to prevent the younger generation from starting the habit of cigarette smoking, and this point was emphasised by Professor Ian Aird, Director, Surgical Unit, Postgraduate

Medical School of London, Hammersmith Hospital, and by Dr. J. A. Scott, Medical Officer of Health, London County Council, in his summing up. Professor Alexander Kennedy, speaking on " The Psychology of Giving Up Smoking," described a number of techniques, including hypnotism and conditioned aversion, to a fascinated audience. He mentioned " Stop Smoking " campaigns with badges to warn others not to provide temptation by offering cigarettes, " Self-Help " circles in which those who had given up smoking could encourage others, and even " No Smoking " holiday camps. Breaking off the habit gradually caused too much psychological tension for too long.

Dr. Julius Wilson, Director, Henry Phipps Institute, University of Pennsylvania, U.S.A., believed that the most probable answer to the controversy about the responsibility of cigarette smoking for the increase in lung cancer was that cancer was due to an unknown cause plus multiple irritants of the bronchial mucosa. Preventive measures must be developed—health education, especially of the young; a change in the chemistry of cigarettes, an effective attack on air pollution, or some means of altering the body's control of cellular growth—some answer must be found.

THE THORACIC SOCIETY

The Summer Meeting was held at the Rigshospitalet, Copenhagen, Denmark, from Wednesday, July 23, to Friday, July 25. The subjects were:

" *Hæmophilus influenzæ* Respiratory Infections," introduced by Philip Allison.

" Incidence of *H. influenzæ* in Bronchitis and Bronchiectasis," Dr. K. Zinnemann.

" Immunological Aspects," Dr. J. R. May.

" Measurement of Lobar or Segmental Function in the Lungs," Dr. P. Hugh-Jones.

" The Operative Assessment of Rheumatic Valve Disease of the Heart," Mr. H. R. S. Harley.

" Thymic Tumours," Mr. T. Holmes Sellors.

" Some Observations on the Use of Tuberculin with Drug Cover in the Treatment of Pulmonary Tuberculosis," Dr. F. H. Young.

" Relaxation of the Diaphragm," Dr. P. Christensen.

" Anticoagulation," Dr. O. Storm.

" Cardiac Arrest," Drs. H. C. Engell, O. Secher and I. Price.

" Late Results of Mitral Valvulotomy," Dr. H. Baden.

" Open Heart Operations," Professor F. Therkelsen and Dr. I. Rygg.

" The Small Intestines as a Reservoir after Total Gastrectomy," Dr. M. Andreassen.

" Closed Operations of Pulmonary Valvular Stenosis," Dr. J. Fabricus and Professor E. Husfeldt.

" X-ray Negative Bronchogenic Carcinoma. An Analysis of 35 Cases seen during 1956 and 1957, with a Special View to the Incidence at the Stage when Patients for the first time seek their Doctor," Dr. Jens L. Hansen.

" Resection of Œsophagus and Cardia," Dr. T. Sondergaard and Dr. P. Ottosen.

" Pre-operative Investigations in Patients with Atrial Septal Defects," Dr. G. Davidsen.

" Diagnostic Punctures of the Heart Cavities," Dr. A. Tybjaerg Hansen.
" Closed Operations for Atrial Septal Defects," Professor E. Husfeldt.
" Cardiac Surgery in Infants," Professor F. Therkelsen.
" Occupational Pulmonary Disease (other than Silicosis) in the last ten years," Dr. K. M. A. Perry.
" The Late Results of Heller's Operation for Cardiospasm," Mr. Frank Nicholson.
" The Action of Pulmonary Hypotensive Drugs," Mr. A. J. Gunning.
" Congenital Obstructive Emphysema," Mr. Charles Drew.
" The Use of a Starling Heart-Lung Preparation as a Pump Oxygenator for Human Blood," Mr. L. J. Temple.

NOTES AND NOTICES

PROFESSOR F. H. SMIRK

We would like to offer our sincere congratulations to the New Zealand member of our Editorial Board, Professor F. H. Smirk, to whom the honour of the K.B.E. was announced in the Birthday Honours List.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE

The Fifth Congress of the International Society of Internal Medicine was held in Philadelphia on April 23 to 26, under the Presidency of Dr. T. Grier Miller. Over 1,000 members and 44 countries were represented, including the U.S.S.R. and Poland.

DEBORAH SANATORIUM AND HOSPITAL

A three-day International Symposium is to be held in Philadelphia under the auspices of the Deborah Sanatorium and Hospital on the status of tuberculosis as a danger to life and the public in general, from Thursday, November 20, to Saturday, November 22, at the Bellevue-Stratford Hotel.

The subjects being introduced are: " Chemotherapeutic Prophylactic Measures for Tuberculosis," by Dr. Sidney Raffel of Stanford University Medical School, San Francisco, California; " The Hospital and Home, Respective Roles in Tuberculosis Management; Chemotherapy of Tuberculosis," by Dr. Aaron D. Chaves, Department of Health, New York; " The Problem of Relapse of Tuberculous Lesions under Chemotherapy and Following Treatment; the Duration of Drug Treatment; the Pathology of Healing Tuberculous Lesions, Bacteriological Problems," by Dr. John D. Steele of the Veterans Hospital, San Fernando, California; " Tuberculosis Case-Finding; the Problem in the General Population, Schools and Hospitals," by Dr. Edward T. Blomquist, Division of Special Health Services, Washington, D.C.; " Surgical Aspects of the Treatment of Pulmonary Tuberculosis; the Type of Operation, Relationship to Chemotherapy, to Bacteriological Status, to Pathology of Treated Tuberculosis," by Mr. F. Ronald Edwards, F.R.C.S., of Liverpool, England; " The Future Problem of Tuberculosis, Programme for its Control," by Dr. Johannes Holm of the World Health Organization, Geneva, Switzerland.

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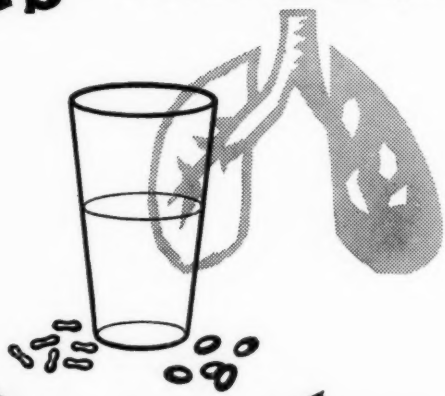

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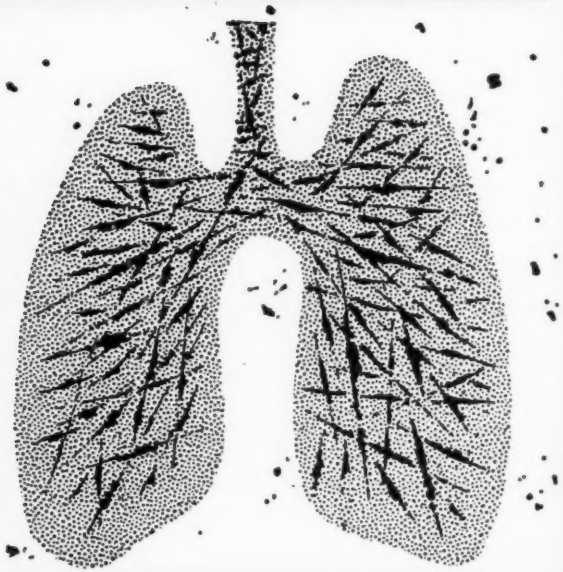

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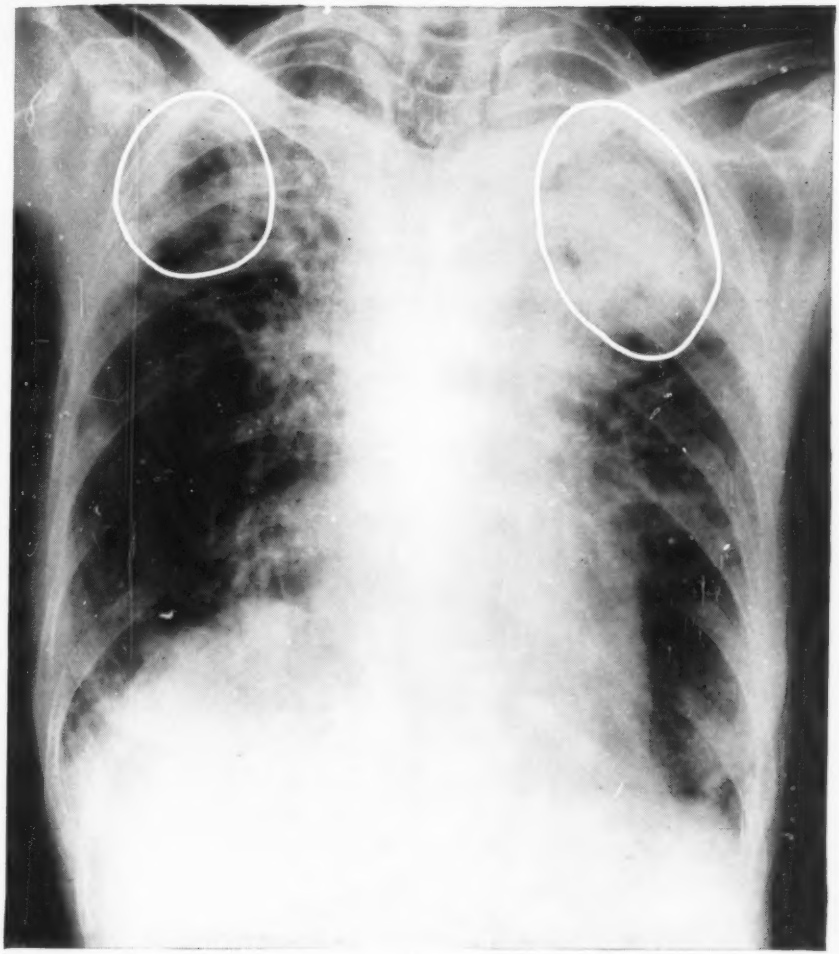

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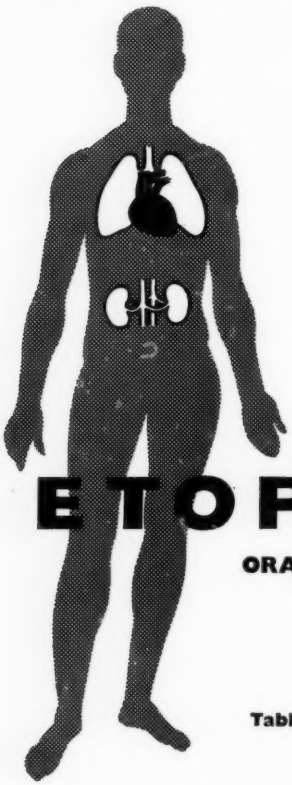

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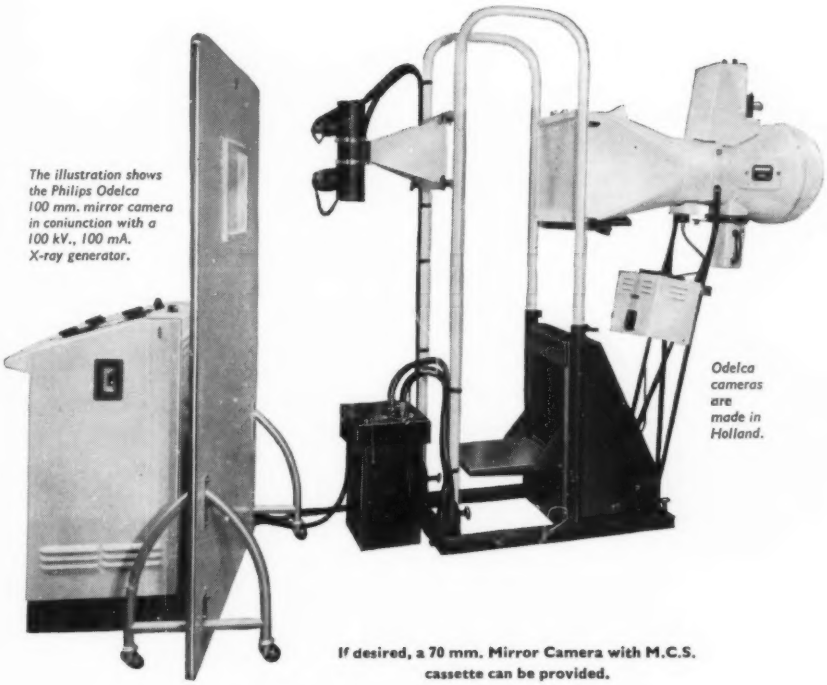

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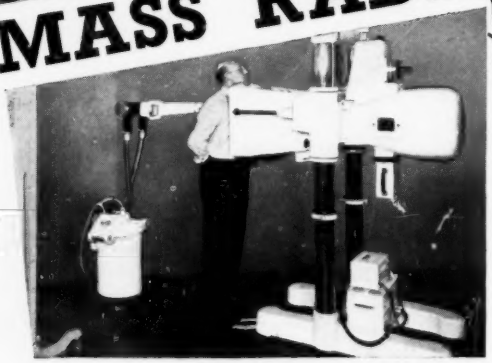

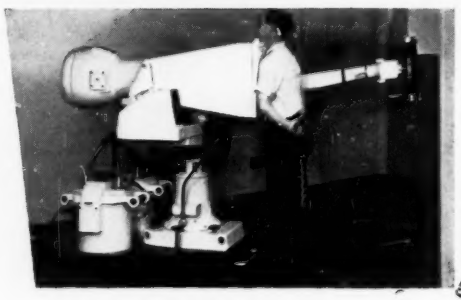

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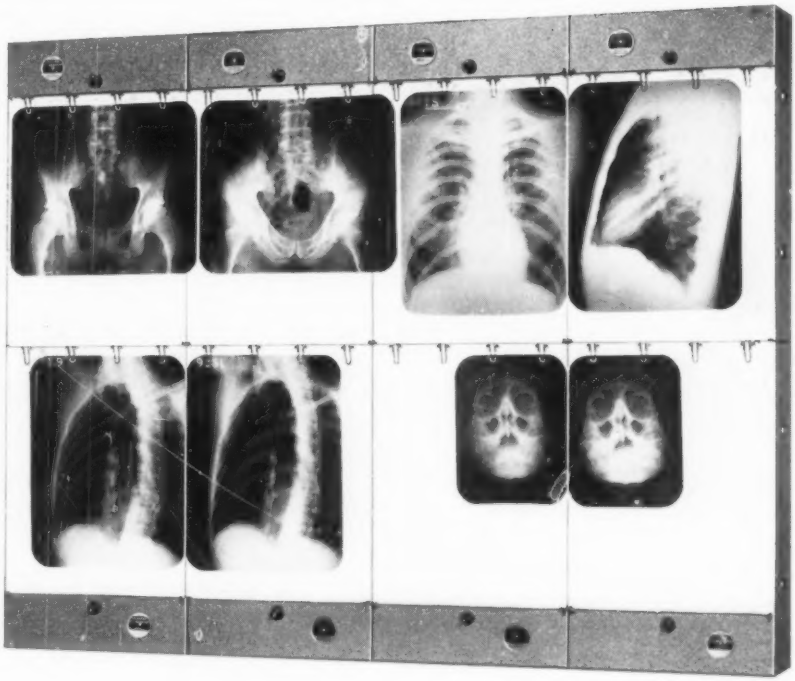

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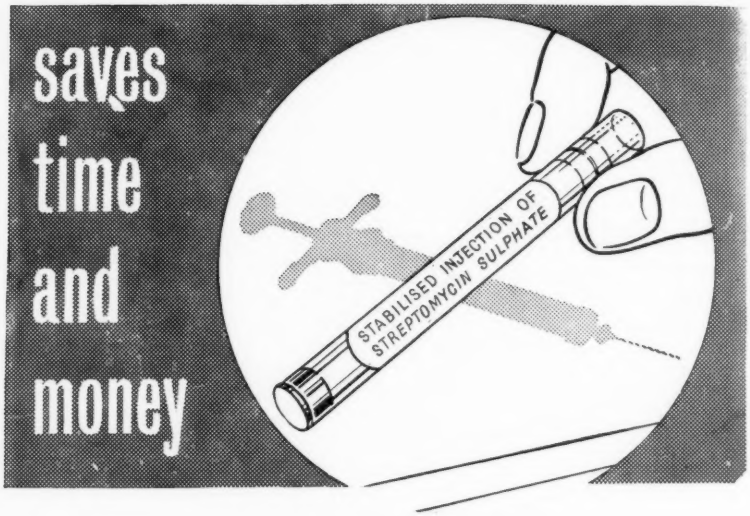

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